THE NEUROANATOMIC CORRELATES OF EMOTIONAL PROSODY IN VERBAL EXPRESSION: A FUNCTIONAL MAGNETIC RESONANCE IMAGING STUDY

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Many lines of investigation implicate the right hemisphere in the comprehension and production of emotional prosodic information, independent of the valence of the prosody, supporting a right hemisphere dominance hypothesis. An alternative valence hypothesis suggests that the production of positive prosody preferentially activates left hemisphere regions and predicts that the production of negative prosody will produce greater right hemisphere brain activity. Functional magnetic resonance imaging (fMRI) was utilized to test these alternative hypotheses and learn more about the anatomic substrate of emotional prosodic production. This recently developed technique is able to reveal anatomic-functional relationships. The brain activity of twelve normal subjects while expressing emotional prosody was examined for right versus left hemisphere differences.

The results of this fMRI study provided supportive evidence of the validity of the right hemisphere dominance hypothesis. It revealed that cerebral activity was greater in the right hemisphere than in the left during the expression of emotional prosody with either positive (e.g., happy) or negative valence (e.g., angry) when compared with that created during the expression of neutral prosody. These findings provide evidence that the right hemisphere has a critical role in the production of emotional prosody. This study also provided tentative evidence that a prosodic output module may be operative in the right frontal region.

CHAPTER 1
INTRODUCTION AND STATEMENT OF THE PROBLEM

Vocal affective intonations play a significant role in communication, but the substrate for this capability is not well understood. To explore these relationships and to reduce the ambiguity of this topic it will be helpful to make a distinction between emotional experiences, mood, and emotional behaviors. Emotional experiences are typically transient, internal states that are difficult to quantify, such as being happy. If these states are more long lasting they are frequently described as a mood, for example being depressed. In contrast, emotional behaviors are the external signs of those internal emotional experiences. These emotional behaviors are used to communicate a person's internal emotional status through facial, postural, or vocal intonations.

Emotional experiences can be categorized by two main factors, valence and arousal. For instance, emotions such as happiness have been described as having pleasant or positive valence, whereas emotions such as anger are described as being unpleasant or having a negative valence. Arousal depicts the range of excitement or intensity (high to low) associated with a particular emotional experience. It is possible to monitor a number of physiological measures that appear to be correlated with emotional experiences, such as changes in the autonomic nervous system affecting heart rate, respiration, or changes in skin conductance. However, it is not known how closely tied these internal emotional experiences are correlated with those quantifiable changes in physiology.

In a similar way, emotional behaviors may or may not be correlated with changes in physiology or alterations in the internal emotional experience. It is impossible to objectively determine the true internal emotional state of an individual and it is conceivable that each observed emotional behavior contains a mix of a genuine emotional experience tied to an observable physiological response, along with a measure of acting. William Shakespeare wrote in As you Like it, act II verse 36, that “All the world 's a stage, and all the men and women merely players. They have their exits and their entrances; And one man in his time plays many parts.” One interpretation of this passage is that Shakespeare proposed that social interactions require the skillful utilization of a wide array of emotional behaviors in an ever changing dynamic.

Within the theatrical community, two main approaches have been utilized to describe the process of acting which involves a conscious manipulation of those emotional behaviors, to elicit the audience’s perception of genuine emotional experiences. Elaborating on earlier development by Stanislavsky (1936), the Strasberg (1987) acting technique known as The Method encourages performers to remember an emotional experience from their past that matches their character’s targeted emotion. They are trained to attempt to re-experience this emotion, incorporating any emotion they are currently feeling, and in the process try to temporarily become the character they are playing.

In contrast, most current performers follow more pragmatic techniques such the Meisner Technique (Meisner & Longwell, 1987) which emphasizes the production of behaviors which mimic the target emotional behaviors, yet they do not attempt to become the character in the process. During a performance it is acknowledged that the actor may or may not actually experience the target emotion, but improvises and produces emotional behaviors that are appropriate to the emotional displays of the other actors. The contrast between these two theatrical techniques can inform studies of emotional behavior. For instance, one must keep in mind the rich sophistication of the human emotional repertoire and that these subtle components are impossible to objectively differentiate. Therefore, while emotional behaviors may be observed and quantified and at times appear be correlated with internal emotional experiences, it remains impossible to prove an actual relationship between the two. At best, the existence of emotional experiences are inferred, based on subjective report and measurements of emotional behaviors.

In spite of this ambiguity, some of the most creative theoreticians of the 19th and 20th century have explored this intriguing human capability (James, 1884). Charles Darwin himself wrote that

> to understand, as far as is possible, the source or origin of the various expressions which may be hourly seen on the faces of the men around us, … ought to possess much interest for us. (Darwin, 1872, p. 360)

Since Darwin (1872), studies of the neural substrates of emotion have revealed that a collection of cortical and subcortical structures known as the limbic system play an important role in emotion. Although portions of the limbic system have a crucial role in supporting emotional processes, these structures do not appear to have an exclusive role. Many believe that both the cortex and the limbic system have a role in emotion processing. Damasio (1994).has argued that emotion may provide a degree of systematic integration which helps individuals interpret the multi-faceted events of everyday life

Left hemisphere injury typically inflicts obvious deficits in language functions (Broca, 1863) yet right hemisphere injuries impose disabilities that are far less readily evident. Right hemisphere injuries impact subtle systems that control visuospatial abilities (Benton, Hannay, & Varney, 1975), attention monitoring capabilities (Heilman and Van Den Abel, 1980), and the comprehension and expression of emotional prosody (Heilman, 1994). Whereas the lexical/semantic aspects of language are typically intact after right hemisphere injury in right handed subjects, the suprasegmental aspects that communicate emotion in the voice, such as prosody, are often deficient (Ross, 1981).

There is evidence (see Locke 1997 for a review) that the initial building blocks of language are prosodic-intonational based on infants' emotional bond to their mother and their attentiveness to the mother's facial expressions (Locke, 1993) and prosodic cues (DeCasper & Spence, 1986). For example, it is known that infants are able to attend and imitate intonation contours in the first six months of life (Masataka, 1992). Perception of these prosodic cues may form a basis for more advanced analysis of segmental components of the speech stream later in development (Goodsitt, Morgan, & Kuhl, 1993; MacNeilage, 1998).

Prosody can also be utilized to convey linguistic information (Behrens, 1988). However emotional prosody, rather than linguistic prosody, will be the focus of this study. Deficits in the production and comprehension of emotional prosody have been documented to occur after right hemisphere injury (Tucker, Watson, & Heilman, 1977; Ross and Mesulam, 1979; Blonder, Bowers, & Heilman, 1991; Blonder, Pickering, Heath, Smith, & Butler, 1995). These deficits in the production of emotional prosody induce a serious functional disability and limit the impact of rehabilitative services (Cummings, 1997; Ween, Alexander, D'Esposito, & Roberts, 1996). However, the brain networks mediating the production of emotional prosody have not been entirely elucidated. Thus, the purpose of the present study was to reveal the physiological substrate of emotional prosody during speech production and in the process evaluate the extent to which this complex system is lateralized.

In this chapter evidence for the neuroanatomical instantiation of emotion through animal modeling and human lesion studies will be reviewed. The system supporting language and speech production in the human will also be briefly discussed. Finally a cognitive neuropsychological model of emotional prosody expression will be described. This review suggested a number of experimental comparisons which were executed to evaluate the validity of the right hemisphere dominance in comparison to the valence hypothesis.

The Emotional Behavior of Prosody

Hughlings Jackson (1932) noted that patients with profound aphasia, even after large left hemisphere lesions, could express emotions through single words by altering the pitch or prosody in their voice. Prosody is a nonverbal or suprasegmental feature of spoken language which conveys various levels of information to the listener. The multiple dimensions of prosody may include pitch, intonation, timing, stress, cadence, tempo, accent, pauses, loudness, timbre, or melody that are delivered along with the lexical-semantic components during language production.

Monrad-Krohn (1947a-b) suggested that there are four different subtypes of prosody: (1) *intrinsic or linguistic prosody* defined as elemental melodic patterns having standard semantic connotations, (2) *intellectual prosody* defined as finely marked intonations that give rise to subtle shades of meaning, (3) *inarticulate prosody* which he described as the use of nonlinguistic speech sounds such as grunts, and (4) *emotional prosody*, an emotional behavior which injects affect into speech and is the focus of this review.

A number of studies have hypothesized that the right hemisphere is more adept at processing the pitch attributes of intonation contours, while the left hemisphere appears to have an advantage in decoding the temporal dimensions of that stimuli (VanLancker and Sidtis, 1992; Pell and Baum, 1997). For instance in a magnetoencephalography (MEG) study of Japanese pitch accents, Imaizumi, Mori, Kiritani, Hosoi, & Tonoike (1998) demonstrated that the left hemisphere is involved in the interpretation of linguistic information irrespective of acoustic cues, while the right hemisphere appears to be involved in the interpretation of prosodic cues. Additionally a left ear (e.g., right hemispheric superiority) advantage has been demonstrated for nonlinguistic stimuli such as music (Kimura, 1964). In contrast, right handed individuals generally demonstrate a right ear advantage (e.g., left hemispheric superiority) for processing linguistic information in dichotic listening tasks (Studdert-Kennedy and Shankweiler, 1970). The explanation for these hemispheric biases typically focuses on the more efficient processing of this information by the respective hemisphere.

Shapiro and Danly (1985) used acoustic analysis to examine patients with right hemisphere damage and tested their ability to produce happy or sad prosody in sentences that were emotionally neutral in content. They found that patients with right anterior lesions spoke with less fundamental frequency variability when compared to non-brain damaged individuals, while those with right posterior lesions produced increased fundamental frequency variability for both emotional and linguistic utterances. When a group of raters (Pell, 1999a) evaluated the emotional prosodic productions (sad, happy, and angry) of 10 subjects with right hemisphere lesions, a substantially greater number of those utterances were misidentified as lacking emotional inflection (e.g., a neutral response was recorded) when compared to utterances produced by normal control subjects. Pell (1999a) noted that the right hemisphere subjects demonstrated subtle difficulties in modulating the fundamental frequency of their emotional prosodic utterances. For instance, the right hemisphere subjects appeared to have difficulty with emotional targets which diverged substantially from a neutral baseline for that vocal parameter. Many have argued that neutral prosody represents an independent point along a prosodic continuum which is then modified through subtle inflection (Grandour, Larsen, Dechongkit, Ponglorpisit, & Khunadorn, 1995; Ladd, 1980). Pell (1999a) concluded that the right hemisphere appears to have an advantage in processing prosodic information which may function in a graded rather than in a categorical fashion (see also Blonder *et al.*, 1995).

Receptive Prosodic Deficits

A number of studies have provided further evidence of a preferential role of the right hemisphere in emotional comprehension. For instance, in 1975 Heilman, Scholes, and

Watson compared six patients with right hemisphere dysfunction and neglect with six left hemisphere patients in an attempt to determine whether prosodic comprehension deficits were preferentially associated with a particular hemisphere. They were presented with emotionally neutral, tape recorded sentences which utilized one of four emotional intonations (happy, sad, angry, indifferent). In half of the trials, the subjects were asked to judge the emotional intonation of the speaker. In the other half they were required to judge the content of the message. Heilman and colleagues (1975) found that both groups of patients were able to correctly identify the content of the sentences. However, the right hemisphere patients had difficulty identifying the emotional intonation of the speaker, while the left hemisphere patients did not. This finding was replicated by Tucker *et al.* (1977; see also Bowers, Coslett, Bauer, Spedie, & Heilman, 1987; Darby, 1993) which supported a role of the right hemisphere in the comprehension of emotional prosody. Barrett, Crucian, Raymer, & Heilman (1999) examined a young woman whose left hemisphere had been almost entirely destroyed following a left carotid artery dissection. After this large left hemisphere injury she was unable to comprehend even simple verbal commands. However, through a test of her prosodic comprehension with visual-prosodic passive matching tasks, it was demonstrated that her comprehension of emotional prosody was intact.

Expressive Prosodic Deficits

While the prior studies demonstrated that right hemisphere injury was associated with a deficit in prosodic comprehension (Barrett *et al.*, 1999; Heilman *et al.*, 1975), prosodic production was not tested at that time. Clinically it has long been known that right hemispheric patients frequently demonstrate flat affect as well as rushed speech in their verbal production. Bell, Davis, Morgan-Fisher, & Ross's (1990) report of deficits in the production of prosody after right hemisphere injury in two school aged children supports a role of the right hemisphere in the production of emotional prosody. In a follow-up to their original study Tucker, Watson and Heilman (1977) examined eleven patients with right hemispheric injuries and compared their performance on tasks of prosodic comprehension and production with seven left hemispheric patients. They documented a significant deficit in prosodic production among the right hemispheric patients and argued that this deficit was a result of lack of access or a damaged prosodic representation (see also Heilman, Bowers, Speedie, & Coslett, 1984). Ross and Mesulam (1979) described two patients with a selective deficits in prosodic production. Based on these findings, and in agreement with Heilman's earlier work (1975), Ross and Mesulam (1979) posited that the right hemisphere was dominant for the coordination of prosodic information and suggested these prosodic representations are stored in this hemisphere.

Explanatory Theories of Prosodic Deficits

The Right Hemisphere Dominance Hypothesis

Ross (1981, 1988) continued to study patients with prosodic deficits and further explored the instantiation of prosodic information within the right hemisphere. He studied ten patients with right hemispheric injury and examined them qualitatively for (1) spontaneous use of affective prosody during conversation, (2) their ability to repeat verbally neutral sentences with affective prosody, (3) their ability to auditorily comprehend affective prosody, and (4) their ability to visually comprehend gestures. He found that the spectrum of aprosodias after right hemispheric injury mirrored the attributes of language deficits with left hemispheric patients. In particular he found the following aprosodias after right hemisphere injury: (1) *motor aprosodia* after damage to the right inferior frontoparietal region characterized by poor spontaneous use of emotional prosody, poor prosodic repetition, and good comprehension of prosody; (2) *sensory aprosodia* after damage to the right posterior superior temporal lobe and posterior inferior parietal lobe characterized by spared spontaneous prosody in conjunction with poor prosodic repetition, and poor comprehension of emotional prosody; (3) *global aprosodia* after damage to right frontal, parietal, anterior occipital, superior temporal lobes characterized by poor performance in spontaneous prosodic production, repetition and comprehension; and (4) *mixed transcortical* after watershed lesions involving the right frontal and parietal lobes extending into the superior temporal lobe marked by intact prosodic repetition with poor spontaneous prosodic production and comprehension.

A cognitive neuropsychological model of language production suggested by Caramazza (1996) posits a hypothesized input lexicon, or module, forming a memory store of words, a semantic system forming a storage network for the meaning of words, and an output lexicon or module which contains the motor behaviors necessary to produce a word verbally. Ross (1981, 1988) conjectured that an analogous system with separate input and output prosodic modules, as well as an emotional semantic system, may also exist. While controversial, this model provides a conceptual framework which has permitted the exploration of a variety of receptive and expressive prosodic deficits across a broad spectrum of patients.

A number of critiques could be applied to Ross's hypothesis (1981, 1988). For instance, the potential role of the basal ganglia in supporting the production of emotional prosody is underdeveloped in his hypothesis and his lesion studies were not examined in detail for damage deep to the cortical surface. Ross (1981, 1988) relied on lower resolution computed topographic (CT) images yet more recent and detailed CT studies (Starkstein, Federoff, Price, Leiguarda, & Robinson, 1994) suggest that patients with receptive prosodic deficits have a higher frequency of right hemisphere lesions which also involved the basal ganglia. Blonder, Gar, and Gur (1989) revealed that patients with both right and left hemiparkinsonism have deficits in producing emotional prosody, suggesting that the neural control on intonation might be bilateral at the level of the basal ganglia. Further evidence is provided by ablation studies of non-human primates. There species-specific calls, which resemble human emotional prosody acoustic structure, appear to be mediated by bilateral, subcortical brain regions (Jurgens, 1979). Support for the involvement of the basal ganglia in prosodic processing also comes from studies of patients with either Parkinson's (Lloyd, 1999) or Huntington's disease (Speedie, Blake, Folstein, Bowers, & Heilman, 1990) which both demonstrated reduced prosodic modulation of speech. Another critique that could be applied to Ross's (1981, 1988) theory relates to his conjecture that the right posterior region is prominently involved in prosodic comprehension, this hypothesis has not been supported by later studies. For instance, George *et al.* (1996) provide *in vivo* evidence in a PET study that comprehension of emotional prosody activates anterior, not posterior, regions of the right hemisphere.

The Valence Hypothesis

An alternative to the right hemisphere dominance theory is the valence hypothesis. This posits that an individual emotion is supported by a particular hemisphere. Many have argued that the left hemisphere mediates positive emotions while the right hemisphere supports negative emotions (Canli, Desmond, Zhao, Glover, & Gabrieli, 1998; Sackeim *et al.*, 1982). This is based on studies such as Starkstein, Federoff, Price, Leiguarda, & Robinson (1987) which revealed that patients with left hemisphere lesions, especially left frontal ones, are often sad, whereas those with right hemispheric injuries are often indifferent. Goldstein (1948) called the depression associated with left hemisphere lesions a catastrophic reaction. This change in mood, most commonly associated with left, but not right hemisphere lesions, may occur because the right hemisphere patients are not exposed to the obvious deficits which left hemisphere patients typically experience such as an aphasia or dysfunction of the preferred hand. Gainotti (1972) proposed that right hemisphere patients experience a greater incidence of unawareness of their deficits (anosognosia), based on their failure to perceive a superficially obvious handicap.

However, Milner (1974) did not find a greater incidence of depression in patients with left hemisphere lesions, and a study by House, Dennis, Warlow, Hawton, & Molyneux (1990) also failed to replicate Starkstein *et al.* (1987) asymmetrical findings.

Canli *et al.* (1998) provided *in vivo* evidence for the valence hypothesis in a fMRI study involving passive viewing of pictures with either positive or negative valence, and reported that viewing pictures with positive valence elicited preferential left hemisphere activity, while pictures with negative valence elicited greater activity in the right hemisphere. Other imaging studies have supported the valence hypothesis and revealed differential lateralization patterns when negative (right frontal) emotions were compared to positive (left frontal) emotions (Imaizumi *et al.*, 1997; Irwin *et al.*, 1997; Paradiso *et al.*, 1997; Sutton, Davidson, Donzella, Irwin, & Dottl, 1997). It remains possible that the task designs of these experiments failed to elicit the target emotions. Others have hypothesized that there is no evolutionary rationale for a neural instantiation of those individual emotions (MacNeilage, 1998).

Possible Neuroanatomic Substrates of Emotional Experiences

While this study will focus on the hemispheric brain laterality of the production of emotional prosody, it is important to briefly review the competing models of emotion experience which inform this discussion. Emotional experience is a complex and multi-faceted human ability and many regions of the brain have been proposed as supporting these capabilities. Many neuroanatomic models have been suggested over the past 100 years, some have been discarded while others have been re-defined.

The Papez Circuit

In 1937 Papez published his influential paper titled “A proposed mechanism of emotion” postulating a central role of the hypothalamus in emotion. This was based on Bard’s (1934) earlier finding that the hypothalamus was involved in the mediation of rage responses. Papez (1937) also postulated a role for the hippocampus, mammillary bodies, fornix, anterior nuclei of the thalamus and the cingulate gyrus in this circuit, because of their connections from the cortex to the hypothalamus. However, later investigations have demonstrated that the Papez circuit, as it has come to be called, is primarily involved with memory. For instance, a severe impairment in new learning was demonstrated after bilateral removal of the medial temporal lobe region (Scoville, 1954; Scoville and Milner, 1957). Later studies (Rempel-Clower, Zola-Morgan, & Squire, 1995; Zola-Morgan, Squire, & Amaral, 1986) demonstrated that even a small bilateral lesion in the CA1(e.g., cornu ammonis) of the hippocampus can induce a marked anterograde memory impairment, without alterations in the patient's emotional experiences or behaviors.

The Basolateral Circuit

Yakovlev (1948) suggested that a basolateral circuit was an important component of the system supporting the expression of emotional experience. Yakovlev (1948) proposed that this circuit included the orbital frontal and insular cortex, the uncinate fasciculus, the anterior temporal cortex, the amygdala and dorsomedial nucleus of the thalamus that projects back to the orbito-frontal cortex. Earlier Kluver and Bucy (1937) had shown that a bilateral lesion of the anterior temporal lobe, including the amygdala, induced placidity in usually aggressive rhesus monkeys. Later Akert, Greusenr, Woosley, & Meyer (1961) demonstrated that the key element in eliminating aggressive behavior was the ablation of the amygdala, rather than the removal of temporal lobe neocortex. Further evidence in support of Yakolev's (1948) proposal came from the finding that stimulation of the amygdala induces rage (Ursin, 1960; Wood, 1956) and bilateral lesions of the amygdala impaired recognition of fear (Scott *et al.*, 1997).

It is tempting to conclude that the human emotional system mirrors that of non-human primates. For instance in humans and in primates there is evidence that the amygdala has an important role in fear (LeDoux, 1993). There are clinical reports of humans who sustained bilateral damage to the amygdala and anterior tempro-cortex which induced the Kluver-Bucy syndrome with blunted emotional reactivity, hypersexuality, hyperorality, and visual agnosia (Lilly, Cummings, Benson, & Frankel, 1983). Additionally impaired comprehension of facial emotions has also been reported after bilateral amygdala damage (Adolphs, Tranel, Damasio, & Damasio, 1994 & 1995).

Whereas the amygdala supports reflexive fear reactions in animals, at issue is the extent to which this reaction becomes modulated in humans who possess more advanced systems that shape this primitive reaction. Halgren (1992) posits that because higher level cognitive inputs are sent to the amygdala, the amygdala may actually have a less crucial role in human emotional experiences than it does in animals. The degree to which cortical resources are engaged in emotional experiences and the extent to which they modulate more ancient brain networks is an important question. Many lines of inquiry support the view that wide expanses of the cortex interpret limbic system output, with suggestions that the right hemisphere has a prominent role in this dynamic (Ross, 1981; Cancelliere and Kertesz, 1990; Borod, Andelman, Obler, Tweedy, & Welkowitz, 1992).

Heilman's Modular Theory of Emotional Experiences and Behaviors

Following a dimensional approach to emotions pioneered by Wundt (1903), Heilman argued that each emotional experience can be described through an understanding of three networks operating in tandem in the brain. Heilman (1994) proposed that these three widely distributed networks support the conscious experience of emotion with one network processing *valence*, a second controlling *arousal*, and a third network mediating *motor activation* with either approach or avoidance behaviors (see also Denny-Brown & Chambers, 1958). He argues that all three of these networks must be taken into account to explain a particular emotional experience of an individual. Heilman (1994) suggested that the different states of these three networks operating concurrently is the best model to understand the variety of emotional experiences of which humans are capable. It is beyond the scope of this text to discuss this theory in detail, but Heilman's (1994) overall framework will be briefly reviewed in light of its potential contribution to a discussion of the neuroanatomic correlates of one emotional behavior, emotional prosody.

Heilman's Valence Network

Heilman (1994) has suggested that while neurotransmitter systems may influence mood, he conjectures that moods and emotions may not be equivalent emotional experiences. He posits that the sadness that has been noted to occur after left hemisphere injury may actually be a result of a modification of these neurotransmitter systems. Starkstein *et al.* (1987) provided evidence that this sadness was associated with lesions in the caudate. They found that the nearer to the frontal pole the lesion was located, regardless of the hemisphere, the more severe was the change in mood. Tucker and Williamson (1984) suggested that these hemispheric valence asymmetries may be related to asymmetrical control of neuropharmacologic systems. For instance they provided evidence that the left hemisphere is more cholinergic and dopaminergic (see also Louilot and Le Moal, 1994; Sullivan and Gratton, 1994), while the right hemisphere appears to be more noradrenergic than the left. Robinson and Starkstein (1989) reported that pharmacological changes after stroke influence the incidence of depression. Using positron emission topography (PET) they reported that right hemispheric strokes increased serotonergic receptor binding while left hemisphere strokes induced less pronounced serotonergic binding. Heilman (1994) concluded that while these neurotransmitter systems may influence mood and valence, the underlying mechanism of this process remains unknown.

Heilman's Arousal Network

Heilman (1994) also posited that emotional experiences are modulated by the general arousal and motivational state of the individual. Perceiving and responding to stimuli require that the organism be awake and alert. The system supporting arousal ranges from the modular cortical limbic reticular network (Mesulam, 1981; Watson, Valenstein, & Heilman, 1981) supporting basic consciousness, to long range planning of goal directed behaviors by the complex, but poorly understood dynamics of the frontal cortices.

Heilman's Motor Activation Network

Emotions are not simply passively experienced but often elicit an active behavioral response. Heilman (1994) proposed that the motor preparatory system, which is engaged when subjects intend to act, is mediated by a widely distributed network guided by the dorsolateral frontal lobe. This system receives input from the limbic system, posterior polymodal association areas and the premotor areas. Lesions of components of this network may all cause akinesia which support its role in motor activation (Watson, Miller, & Heilman, 1978). Coslett and Heilman (1989) demonstrated that right hemisphere lesions are more likely to be associated with contralateral akinesia than left hemisphere lesions. Furthermore Heilman (1994) posited a preferential role for the right hemisphere in intention (Coslett and Heilman, 1989). Patients with parietal lesions, especially right sided lesions, may fail to move or move slowly in the space opposite the parietal lesion.

Heilman (1994) argues that the right hemisphere has a preferential role in the expression of emotional behaviors. While the three networks Heilman (1994) discusses appear sufficient to depict the global, over-arching systems supporting emotional experiences and some aspects of emotional behavior, his proposal does not specifically address the mechanisms which facilitate the verbal expression of emotion. It will be beneficial to examine this intricate system in more detail, in light of its involvement in prosodic production.

Verbal Expression

As noted earlier there are multiple modalities through which humans express emotion. Facial expressions were detailed in Darwin's (1872) investigations, but verbal expression is also used extensively in social interactions to express internal emotional experiences. The process of speaking involves multiple systems which have been shown to fractionate after neurological injury (Caramazza, 1996). These multiple components include the motivation to speak or intentionality as elaborated in Heilman's (1994) conceptual framework, the coordination of the oral musculature, on-line construction of lexical/semantic components into phrase length segments and the process by which prosodic nuance is superimposed on this lexical/semantic content to express the emotional status of that individual. It will be helpful to examine these different aspects of verbal expression separately.

Animal Models of Vocal Expression

Only man utilizes spoken language and as such examining vocal behavior, even among the higher primates, is not an equivalent process. However, detailed experimental manipulations with selective lesions and pathway tracings is ethically permissible with these higher mammals and this has revealed a great deal about the neuroanatomic basis of the motoric aspects of vocal production.

From a review of this animal literature, Farley (1989) argues that there are four main motor systems that control vocal tract motor neurons in the human. The first is a respiratory control system which maintains physiological blood-gas levels. The second is an vocalization system which may also have an emotional dimension.

This utilizes portions of the anterior cingulate and the periaqueductal gray area. Adametz and O'Leary (1959) reported that periaqueductal lesions in cats induced mutism and Jurgens and Pratt (1979a) revealed that lesions in the periaqueductal gray area abolished species-specific calls in squirrel monkeys (see also Bandler & Shipley, 1994). In non-humans it appears that this vocalization system supports calls of distress, which can be produced even in decerebrate animals (Carrive, Dampney, & Bandler, 1987). Third Farley (1989) discusses a general motor system involving the basal ganglia, motor thalamus, cerebellum, and cortical motor systems. Finally, he adds higher order cortical control centers which are operative only in humans, such as Wernicke's and Broca's areas.

The Frontal Lobes

The Anatomy of the Frontal Lobes

The frontal lobes are a complex, but not well understood portion of the brain which receive a rich and complex assortment of inputs from a variety of other brain regions (see Damasio and Anderson, 1993 for a review). Within each hemisphere three main frontal regions have been delineated: (1) the precentral cortex (Brodmann's area 4), a thin ribbon of tissue just anterior to the rolandic fissure, (2) the premotor region, encompassing a larger area anterior to the motor strip including lateral and medial regions (Brodmann area 6), and (3) the vast prefrontal region anterior to the premotor cortex (Brodmann areas 8-12, 46, and 47) including limbic cortices as well (Brodmann's areas 24, 25, and 32).

Layers II and III of the precentral cortex contains large Betz cells whose axons descend to the spinal cord. However only half of the corticospinal fibers originate in this region, with the other half coming from the premotor and supplementary motor areas (SMA) (Pandya and Barnes, 1987). This well organized projection is in contrast to the multi-faceted network which engages the prefrontal region. This area, which expanded dramatically during mammalian evolution (Sanides, 1969), has direct or indirect interconnections to all the other cerebral lobes via long association bundles. It also receives input from varied sources such as (1) the limbic system, (2) the reticular system, (3) the hypothalamus, and (4) neurotransmitter systems such as the ascending noradrenergic fibers originating from the locus ceruleus located in the pons. This prefrontal region is the only known area of cortex to receive strong projections from all of these regions (Stuss and Benson, 1986).

The Function of the Frontal Lobes

The function of the precentral area (Brodmann's area 4) is strongly associated with the direct facilitation of basic motoric functions. Electric stimulation of Brodmann area 4 in awake subjects produces small movements of one muscle or a small group of muscles on the contralateral side of the body (see Penfield and Rasmussen, 1950 for a review). However stimulation of the premotor area produces movements of much larger groups of muscles, with supplemental motor area (SMA, Brodmann's area 6) stimulation eliciting more complex movements. Therefore the premotor area has been hypothesized to be involved in the coordination and planning of complex motoric sequences (Roland, Larsen, Lassen, and Skinhoj, 1980). However, while the basic functions of the motor and premotor areas have been elucidated, the function of the prefrontal region is much more enigmatic (Cavada and Schultz, 2000).

The prefrontal region has been further subdivided into (a) a dorsolateral region, (b) an orbitofrontal region, and (c) a frontal medial region. While the orbitofrontal region appears to have a role in decision-making (Bechara, Damasio, Damasio, & Anderson, 1994; Damasio, Tranel, & Damasio, 1991), and inhibition (Roberts & Wallis, 2000), it also appears to have a role in the interpretation of emotional stimuli (Bechara, Damasio, & Damasio, 2000) and has prominent limbic connections (Damasio and Van Hoesen, 1983). Lesions in this orbitofrontal region are known to produce personality changes (Rolls, 1996). The dorsolateral region of the prefrontal lobes appears to have a more prominent role in cognitive tasks such as verbal fluency (Benton, 1968), associative learning (Petrides, Alivisatos, Evans, and Meyer, 1993), and the inhibition of some behaviors (Diamond, 1989; Drewe, 1975; Luria, 1966). While the frontal medial region appears to be more involved in motoric intention with lesions in this region producing mutism, motoric preservation or impersistence (Heilman and Watson, 1991). There is evidence that this large prefrontal region is involved in coordinating complex behavior through these parallel inhibitory and excitatory pathways to which they are connected (Knight, Staines, Swich, and Chao, 1999).

The Role of the Frontal Lobes in Language and Emotional Processing

Since 1861 when Paul Broca reported a patient whose speech was limited to a single syllable after a left posterior inferior frontal lesion, a preeminent role for the production of language has been attributed to the left frontal region. Later studies of other patients with left hemisphere lesions have continued to support the hypothesis that multiple language capabilities such as syntax, phonology, and lexical semantics are preferentially located in this dominant hemisphere (Damasio, 1992).

Adametz and O'Leary (1959) and Jurgens and Pratt (1979a) demonstrated that lesions in the supplementary motor area in the frontal cortex of animals induces the cessation of species specific calls. Correspondingly, human patients who have experienced lesions in their left supplementary motor area have demonstrated difficulty with vocal production, which has been termed transcortical motor aphasia. This language deficit is defined by decreased initiation of spontaneous speech, with a very slow rate of speech production. Additionally, if their lesion was large and extended through the medial frontal area, a profound akinetic mutism has been noted to occur (Barris & Schuman, 1953; Damasio & Anderson, 1993; Goldburg, 1985; Nielson and Jacobs, 1951). As a result many attribute the initiation of language production to these regions (Benson, 1993; Rothi, 1990). Many functional neuroimaging studies have also implicated the medial frontal cortex in word generation tasks (Crosson *et al.*, 1999a; Friston *et al.*, 1991; Warburton *et al.*, 1996) or language monitoring tasks (Binder *et al.*, 1997). Other studies have replicated the classic lesion studies with neuroimaging paradigms and have documented that the left dorsolateral frontal cortex plays a role in semantic access during a word generation task (Crosson *et al.*, 1997; Frost *et al.*, 1999; McCarthy, Blamire, Rothman, Gruetter, & Shulman, 1993; Petersen, Fox, Posner, Mintun, & Raichle, 1988) and in tasks which require a semantic decision (Demb *et al.*, 1995; Gabrieli, Poldrack, & Desmond, 1998).

Broca's and Wernicke's areas (Brodmann's areas 44/45 and parts of 22/39/40 respectively) in the left hemisphere of normal right handed subjects are complex cortical regions whose functioning is still not well understood (Caramazza, 1996; Damasio, Grabowski, Tranel, Hichwa, & Damasio, 1996. Caplan, Albert, & Waters, 1999). Many envision that Broca's and Wernicke's areas are the nexus of multiple parallel distributed processing (PDP) language networks (Dell, 1986). The classic Wernicke-Geschwind paradigm posits their respective role in speech production and comprehension, however an evolving conceptualization suggests that it is more likely that both of these areas are two poles along a perisylvian continuum which perform incremental language processing tasks along its cortical expanse (Anderson *et al.*, 1999) potentially even engaging widely separated brain regions in this process (Damasio *et al.,* 1996; Mesulam, 1998).

The precise role of Broca's area in language production remains controversial (Goodglass, 1993; Zatorre, Meyer, Gjedde, & Evans, 1996). For instance, there is evidence (Foundas, Eure, Luevano, & Weinberger, 1998) that Broca's area can be fractionated into two functional areas. A anterior part (Brodmann's area 45, pars trianguluaris) likely related to lexical retrieval, and a posterior part (Brodmann's area 44, pars opercularis) with mainly motor articulatory functions. In fact, Tauber, Raymer, and Heilman (1999) reported a patient with a dominant frontal operculum lesion which also damaged the adjacent premotor and primary motor cortex and demonstrated symptoms consistent with a transcortical motor aphasia. This aphasia is more commonly associated with SMA and anterior cingulate lesions (Atkinson, 1971). Lecours and Lhermitte (1976) noted that a dominate opercular lesion induced a profound phonetic disintegration impairing communication. Therefore this evidence suggests that while speech production does engage Broca's area (Brodmann's areas 44 & 45) as classically described, it does so in conjunction with these associated premotor and primary motor cortex regions (Wildgrubber, Ackermann, Klose, Kardatzki, & Grodd, 1996).

It is clear from a vast body of literature that the production of lexical/semantic aspects of language production emanate from the left frontal region. As a consequence any task requiring speech production will engage this region, whether prosody is produced in the speech production or not. What has not been determined is why the left frontal lobe is engaged during this task and additionally what role the right frontal cortices may have during the expression of emotional prosody.

While the actual function of these frontal regions are still debated, any neuro-imaging experiment which requires an overt verbal response, will undoubtedly reveal brain activity due to the engagement of what Pinker (1994) has termed *the language organ.* Additionally if the task requires the production of emotional prosody this may be sufficient to engage emotionally related cortices and to produce pitch changes in the voice motorically related cortices will likely be engaged. The challenge is to somehow isolate the activity due exclusively to prosodic production, from that associated with language production more generally. Specific methods to accomplish this goal will be discussed later in this dissertation.

The Neuroimaging of Emotion and Prosody

As noted earlier, it is impossible to objectively determine whether a subject is actually experiencing a target emotion during an experimental trial. It has also been methodologically difficult to create experimental paradigms which induce robust and reproducible emotional states. Additionally the technical instruments themselves impose their own set of limitations.

For instance, functional magnetic resonance imaging (fMRI) while having greater temporal and spatial resolution when compared to positron emission topography (PET), has a low signal-to-noise ratio, is very susceptible to motion artifacts, and provides a noisy and distracting testing environment. Typically fMRI studies have utilized a blocked paradigm which requires the subject to perform a experimental task, such as finger tapping, continuously and repeatedly for a period of time. For instance, 15 seconds of finger tapping is then followed by a block of 15 seconds of rest as a control comparison state. This control state often has been rest, though other more active tasks have been used as control states. This cycle is then repeated many more times to increase the number of trials and hence increase the statistical power of the analysis. Then each individual voxel monitored during the experimental period is compared to the same voxel also monitored during the control period. Those voxels that are significantly different between the experimental and control blocks are then colorized and overlaid onto a structural MRI image.

The majority of fMRI studies have utilized this simple blocked paradigm approach with great success, and this approach appears to be sensitive to a wide range of motoric and cognitive tasks. However, one problem with blocked fMRI studies is that other lines of inquiry indicate that cognitive tasks such as reading or lexical access (Posner and Abdullaev, 1999) are swiftly processed on the scale of milliseconds. The blocked technique may not have sufficient temporal resolution to reveal these very rapid brain events. This problem is compounded by an issue which effects all fMRI studies. It is known that the repeated trials (necessary to boost the statistical power of the analysis) have the potential to reduce the amount of brain activity visualized because of habituation or the subject's inattention to the target behavior.

Even with these difficulties a number of studies have been reported which have explored the neuroanatomic correlates of emotion and prosody. For instance, Phillips *et al.* (1997) reported the findings from their fMRI study which revealed amygdala involvement during the perception of fearful faces. Beauregard *et al.* (1997) in a PET study compared the patterns of brain activity associated with the passive viewing of words with either neutral (animal names) or emotional connotations. They reported that the passive viewing of words with emotional connotations, when subtracted from a control task of viewing plus signs (e.g., +), elicited brain activity in the right frontal and midline orbital frontal region. Additionally they reported activity in the left inferior and middle frontal gyri arguably due to the language demands of the task. Maddock and Buonocore (1997) utilized passive listening of threat related words contrasted with passive listening to neutral words in a blocked fMRI experiment which revealed left posterior cingulate gyrus activity in eight of the 10 subjects. In a PET study Lane *et al.* (1997) demonstrated that the passive viewing of emotionally evocative pictures, contrasted with passive viewing of emotionally neutral pictures, revealed activity in bilateral prefrontal area (Brodmann's area 9) for pictures with either positive or negative valence. In general, these findings support some role of this prefrontal region in tasks which involve lexical access or emotional processing, but the specific regions engaged in each task are still underspecified.

Crosson *et al.* (1999b) in a fMRI study provided evidence that covertly generating words with emotional connotations engaged cortex near the left frontal and temporal poles, when compared to generating emotionally neutral words. Crosson and colleagues (1999b) hypothesized this occurred because these regions were involved in processing semantic attributes of those words, that is, their emotional connotation. It is important to note that due to technical limitations Crosson *et al.* (1999b) monitored brain activity in only the left, not the right, hemisphere during these tasks and that their emotional word generation task alternated between cues with positive as well as negative valence.

As noted earlier, Canli *et al.,* (1998) examined activity in both hemispheres in a fMRI study involving passive viewing of pictures with positive emotional valence contrasted with pictures with negative valence. They reported that pictures with positive valence preferentially elicited left middle frontal gyrus activity, as well as left middle and superior temporal gyri. However, when viewing pictures with negative valence Canli and colleagues (1998) reported activity in the right inferior frontal and in the gyrus rectus in the orbitofrontal lobe. This provides some support for the earlier described valence hypothesis, but it does not address the issue of emotional prosodic production.

More specific to the neuroanatomic correlates of emotional prosody, George *et al.* (1996) explored whether normal subjects would show differing patterns of brain activity in their right hemispheres during a PET study while they were engaged in comprehending emotional prosody with either positive or negative valence. They found that listening to emotional prosody (with either happy, sad, or angry prosody) preferentially activated the right prefrontal cortex, while comprehending neutral declarative sentences activated the prefrontal cortex bilaterally, on the left more so than on the right. Furthermore Pihan, Altenmuller, & Ackermann, (1997) in an EEG study with 16 normal subjects also reported that when the subjects listened to emotional prosody, a significantly lateralized negativity towards the right hemisphere was revealed in the EEG signal. It is important to note that the George *et al.* (1996) findings involved averaged functional data across his 13 subjects, and that the spatial resolution of PET and the EEG technique used in the Pihan *et al.* (1997) study was quite limited.

No previous fMRI studies have examined the neuroanatomic correlates of the overt production of emotional prosody. One factor is that overt speech production easily induces movement artifacts in fMRI studies. However recently developed fMRI techniques which utilize event-related techniques (Birn *et al.*, 1999a-b; Buckner *et al.*, 1996; Rosen, Buckner, & Dale, 1998) show promise of revealing the patterns of brain activity associated with the production of emotional prosody on the individual subject level across both hemispheres. A more in-depth discussion follows in which the technical aspects of the fMRI experimental scans and the rationale for the use of this particular neuro-imaging technique is discussed.

fMRI - Functional Magnetic Resonance Imaging

The neuro-imaging technique of fMRI provides a non-invasive method to explore brain/behavior relationships *in vivo* with either normal subjects or subjects with neurological disease. While studies based on patients with cerebral dysfunction are of great value, it is also true that the anatomy of the resulting damage often depends more upon the vascular anatomy of the brain, rather than the functional networks operating within it. Functional MRI provides a method by which the regional cerebral blood oxygenation related to a cognitive task can be visualized. This is based on the BOLD (blood oxygenation level dependent) technique related to changes in magnetic susceptibility related to the volume of deoxygenated blood in task-related brain regions (Frostig, Lieke, Ts, & Grinvald, 1990),. Since its inception in 1991 (Belliveau *et al.*, 1991), fMRI has shown promise of depicting changes in the relative volume of deoxygenated blood volumes associated with cognitive tasks in a safe and non-intrusive fashion.

Early fMRI studies utilized a blocked paradigm (Bandettini, Jesmanowicz, Wong, & Hyde, 1993) in which the subject performed a task during an active period, for example finger tapping as rapidly as possible during a 15-second period, and then they were cued to lie quietly for the next 15 seconds during a rest period. This active/rest cycle was then repeated a number of times in order to improve the low signal-to-noise ratio of the MRI signal. Then during processing after the scan had been completed, comparisons would be made between the active versus rest cycles in individual voxels to visualize the additional brain activity that was occurring as a result of the demands of finger tapping. If the subject had not moved excessively during the scan, and the computations had been set up correctly, the result would produce a map of cerebral brain activity that occurred during the execution of the finger tapping task, above and beyond the baseline activity associated with the rest period (see Figure 1).

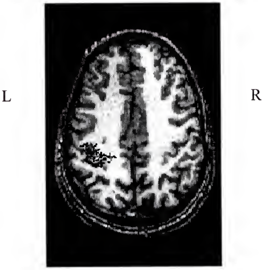


Figure 1. Cerebral brain activity in the left motor cortex associated with a right thumb to index finger tapping task depicted in the axial plane from a preliminary fMRI motoric experiment (Anderson *et al.*, 1998).

This blocked technique was initially utilized in tasks which activated primary visual or motor cortices and this was later expanded to examine more subtle cognitive paradigms such as higher order language, memory, or visuo-spatial abilities. Subsequent fMRI statistical development has provided other options such as statistical parametric mapping (SPM; see Friston *et al.*, 1995), motion correction algorithms (Woods, Cherry, & Mazziotta, 1993) and event related techniques (Friston *et al.*, 1998).

Development of scanner technology has created advancements in the speed of acquisition of the MRI signal which has permitted larger volumes of the brain to be monitored. For each fMRI protocol, choices must be made between the spatial resolution that is required for each experiment, the speed at which a single image is acquired, and the size of the datasets that will be created from a single functional scan. The size of the datasets is important because while the high-end Unix workstations can easily manipulate this large collection of files that are typically produced with a single subject, the older clinical MRI scanners that are utilized for research often have insufficient memory for this task.

There are now a number of statistical, computational approaches that an fMRI investigator may choose to examine their data. One such program developed by Cox (1996) at the Medical College of Wisconsin in Milwaukee, called AFNI (Analysis of Functional Neuro Imaging), is an integrated software package (see Figure 2) which provides a number of statistical options for data analysis such as a correlational comparisons of the change in the MR signal with a reference wave or t-test comparisons between different functional scans (Bandettini *et al.*, 1993). For example, in the earlier discussion of a finger tapping task, a sinusoidal reference wave was utilized which depicted the presumed high levels of activity in the contralateral motor area associated with finger tapping, contrasted with low or baseline levels of activity in the motor area during the control period when finger tapping was not occurring.

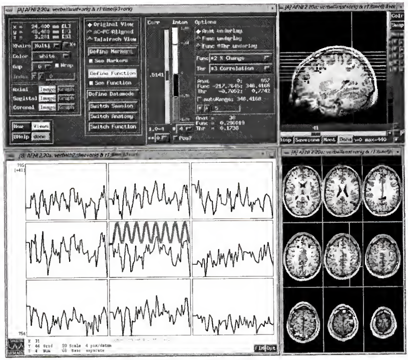


Figure 2. Screen shot of the Unix-based software program AFNI.

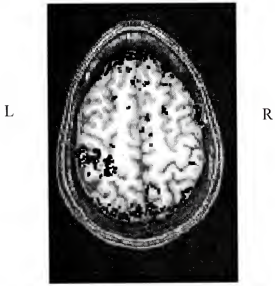


Figure 3. Artifactual cerebral activity is present in the anterior and posterior regions of this axial image, likely correlated with head movement during task performance. This right thumb to index finger tapping task also revealed probable task related activity in the motor cortices of the left hemisphere from this preliminary fMRI experiment (Anderson *et al.*, 1998).

Overt vs. Covert Expression

Many neuro-imaging investigators have pursued language studies which utilized covert, as opposed to overt, verbal expression paradigms because of the problem of motion artifact in overt experiments secondary to head motion (Friedman *et al.*, 1998; Phelps, Hyder, Blamire, & Shulman, 1997; Zelkowicz, Herbster, Nebes, Mintun, & Becker, 1998) or the desire to eliminate the possibility of hearing one's own voice (Warburton *et al.*, 1996). PET covert naming trials have shown that similar left perisylvian areas are activated when compared to overt naming trials (Salmelin, Hari, Lounasmaa, & Sams, 1994). However, the covert trials demonstrate somewhat decreased volumes of activity overall, especially with respect to activity in the left frontal region. This covert naming technique has facilitated the creation of a large body of studies. However, overt and covert behaviors are different. If subjects move their head during speaking, even if only slightly, disruptions in the acquision of the MRI signal and artifactual activity is produced (see Figure 3). Additionally, it is known that overt speech, which requires the movement of air through air filled cavities just inferior to the orbitofrontal cortex, may lead to a reduction in the signal-to-noise ratio through the creation of regions of hyper- or hypo-intensity in the raw MR signal (Birn, Bandettini, Cox, Jesmanowicz, & Shaker, 1999a; Birn, Bandettini, & Shaker, 1999b). However, a number of techniques have been developed that show promise of overcoming this inherent limitation of fMRI.

T-test analysis

For instance, it is possible to utilize a Student t-test analysis which would compare activation from one period or epoch of a trial when the hemodynamic response has peaked in engaged cortices to another epoch when the hemodynamic response should have returned to a baseline level of activity. This pseudo-event related technique has the potential of reducing the artifactual activation related to speaking by eliminating the data gathered when the subject was speaking (see Figure 4). It would be optimal to reveal individual patterns of task-related brain activity, however a recent article by Barch *et al.*, (1999) while validating the use of overt speech production in a fMRI experimental paradigm, strongly recommended the use of averaged group statistical analysis because of variable responses at the individual subject level.

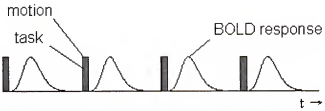


Figure 4. Motion artifact occurs during speaking (solid bars) during the brief initial time period, while the BOLD MRI response due to speaking evolves over a longer duration.

Purpose of the Study and Hypotheses

In summary, this review provides evidence that: (1) Emotional prosody is an integral component of verbal expression, with the limbic system and the frontal lobes playing an important role (Tucker *et al.*, 1977; Ross and Mesulam, 1977; Maddock and Buonocore, 1997). However, it is also clear that cortical association areas also modulate and interpret these emotional experiences. It is still controversial whether the right hemisphere has a preferential role in this function as the right hemisphere dominant theory stipulates. Alternatively emotions may be bilaterally facilitated as the valence hypothesis suggests, with the right hemisphere mediating negative emotions and the left positive emotions. (2) The neuroanatomic location of the systems supporting language and emotional prosody are complex and not easily separated by either ablation or neuroimaging paradigms. For instance, ablation studies have provided the strongest evidence for the neuroanatomic location of these functions, but functional activity is poorly mapped across typical lesion distribution patterns which appear to reflect hemodynamic, rather than functional factors. Initially, neuroimaging technologies such as PET aided investigations of the specific substrates of language and emotion, but the poor spatial resolution of this technique has limited the anatomic precision of these investigations. The more recent *in vivo* neuro-imaging methodology of fMRI shows the greatest promise of revealing these anatomic-functional relationships with even more specificity than PET or ablation studies. However, new fMRI approaches will need to be utilized to address the multiple, conflicting demands of: (a) permitting overt production of speech prosody while avoiding motion induced artifact, (b) providing sufficient brain coverage to permit comparisons between hemispheres along with rapid acquision of MR images, (c) generating a sufficient number of trials to offset the poor signal-to-noise ratio of fMRI, yet retaining the subject's attention throughout those multiple trials to avoid habituation or inattention resulting in a decrease of brain activity. (3) From a cognitive neuropsychological perspective it is possible that a prosodic output module may exist which can be independently damaged. However, the neuroanatomic substrate for a hypothesized system that mediates the expression of emotional prosody has been only tentatively established. Based on the preceding review a number of questions remain unanswered.

Research Question 1

Does the experimental evidence support the validity of the right hemisphere dominance hypothesis, the valence hypothesis, or a third alternative? That is, if a group of subjects express emotional prosody during overt verbal expression in a fMRI experiment, will this preferentially activate the right hemisphere (independent of the valence of the emotion) in support of the right hemisphere dominance hypothesis, or alternatively will the hemispheric brain activity recorded be dependent on the valence of the emotional prosody in support of the valence hypothesis?

Research Question 2

Is there any evidence for the existence of a prosodic output module in the right frontal lobe and can a cognitive model of prosody production be generated from this information? Ross (1981) provided evidence that lesions in the right frontal lobe induce deficits in the expression of emotional prosody. From a cognitive model of prosody production, it is possible that a hypothesized output module exists in the right frontal lobe which stores motoric representations of emotional prosody activated during verbal production. If this assumption was correct, greater activation of the right frontal lobe would be present during neuroimaging tasks which required prosodic expression.

A priori Prediction Research Question 1

It was predicted that an fMRI experiment would provide greater support for the right hemisphere dominance hypothesis when the production of emotional prosody was compared to neutral prosody production. It was assumed that prosody vs. null hypothesis comparisons would induce substantial left hemisphere brain activity as a result of lexical/semantic demands, but these would be minimized when compared to neutral prosody. This finding would challenge the valence hypothesis and lend support to the right hemisphere dominance theory.

***A priori* Prediction Research Question 2**

It was predicted that the results of this experiment would reveal activity in the right frontal lobe during the production of emotional prosody, which would provide tentative evidence for this hypothesized prosodic output module. This was based on ablation studies (Ross & Mesulam, 1979; Tucker, Watson, & Heilman, 1977) which noted that right frontal lesions induced a deficit in prosodic expression. It was assumed that only limited evidence for a cognitive model of prosody production would be provided by this study.

CHAPTER 2
METHODOLOGY

Subject Screening Measures

Twelve (six male and six female) right handed subjects between the ages of 18 and 45 who were recruited from the University of Florida academic community to take part in this study. Subjects were screened prior to their participation in the study and filled out a number of questionnaires which determined: (1) handedness, as determined by the revised Waterloo Handedness Questionnaire (Steenhuis and Bryden, 1989) and the Briggs & Nebes Handedness Inventory (Briggs and Nebes, 1975); (2) languages spoken and age of acquisition; (3) evidence of depression (Beck Depression Inventory; Beck, 1987) and past neurological history; and (4) educational background. Potential risks of the experiment were explained to all subjects and each gave written informed consent in compliance with the University of Florida's Health Center Institutional Review Board guidelines. Criteria for exclusion from this study included: a less than strongly right handed on the Waterloo Handedness Questionnaire bias (a score of less than 52 out of a possible 72), the initial acquisition of a language other than English, any history of a psychiatric disorder (DSM IV), evidence of depression which might limit a subject from expressing emotional prosody, any developmental learning disorder including attention deficits/hyperactivity disorders (ADHD), or a prior neurological injury. While education was noted, it did not serve as an exclusion criteria.

The Waterloo Handedness Questionnaire provided subjects with 36 questions such as “Which hand would you use to adjust the volume knob on a radio?” with an *always right hand* response receiving a +2 score, a *usually right hand* response receiving a +1 score, a *either hand* response received a 0 score, while a *usually left hand* response received a -1 score and an *always left hand* response received a -2 score. The scoring system for the Briggs and Nebes Handedness Inventory utilized the same scoring system as the Waterloo Handedness Questionnaire.

The Beck Depression Inventory (1987) provided subjects with 21 groups of four printed sentences. The task was to choose one sentence among each group of four which best depicted their emotional state over the past week. One of these four potential responses was not related to depressive symptomology such as “I am not particularly discouraged about the future” while each of the other three in each set had an advancing degree of depressive symptomology. The sentence without a depressive tone was scored 0, the sentence with the mildest depressive relatedness would have received a score of +1, and so on. The sentence that expressed the greatest degree of depression in each set would have received a score of +3.

After the handedness and depression measures were completed and the history had been recorded, individuals who were admitted as study subjects performed the three control measures and the experimental tasks that day. Each control and experimental task is described separately below.

Control Measures

Subject responses during the experimental tasks, administered within the scanner environment, could have varied due to a number of factors that were unrelated to the target task of producing emotional prosody. Therefore a number of control measures were utilized to reveal these potential sources of variability that could have influenced their performance. For instance, it is possible that subjects would have been distracted by the loud, confining environment of the scanner. This environment could also have induced anxiety which potentially would have limited the extent to which they could have sounded and felt happy. Therefore *Control Measure 1* audio recorded the subject's spoken responses in the scanner to allow the opportunity to describe the prosody of each subject during experimental testing and this was later compared to the subject's prosodic production outside of the scanner environment. Due to the loud acoustic environment in the MR scanner, the subject's actual prosodic production might still not have been recordable. Therefore the subject's production of emotional and neutral prosody outside the scanner environment was evaluated in free field testing.

Furthermore, even if the subject's production of emotional prosody matched the target provided during the experimental task, they might still have actually experienced a different emotion during the trial. Therefore *Control Measure 2* provided each subject with a questionnaire which they filled out after the scan had occurred to probe their subjective perception of their prosodic production during the experimental trials. The particulars of each of these control measures are described below.

Control Measure 1: Prosody Production Within and Outside of Scanner

During the scan, the subject's responses were audiotaped to document the subject's correct production of the target prosody. To ensure a consistent response across subjects, each subject received a five minute training about the timing and intensity of their verbal response while in the scanner environment. Subjects were instructed to produce the spoken sentence with their normal conversational voice and speech volume. During the production of emotional prosody subjects were encouraged to produce a level of emotional intensity that would be natural for them to utilize during social conversations. It was suggested that they attempt to experience the cued target emotion during the experimental trials. During all trials subjects were instructed to minimize head movement during speaking.

To assess the subject's performance outside of the scanner environment, 18 trials of prosodic productions in free field testing were also performed. Six trials each of positive, negative, and neutral valenced prosodic renditions of the same target sentence used in the scanner during experimental testing, namely, "They went to the store" were recorded to assess the subject's prosodic accuracy outside of the distracting, anxiety-provoking environment of the scanner.

The in-scanner recording was made possible by a specially adapted bi-directional dual microphone (Jabra Corp, San Diego, CA) which minimized the background sound of the scanner by phase reversing the waveform associated with this sound and subtracting it from the speech and scanner signal. Free field testing was recorded (Sony model TCM-323 CE7) utilizing the built-in microphone onto audiotape (Maxell model C90) in a quiet room after the scanning session. The microphone was six inches from the mouth and this was consistent across all the subjects. These audiotape recordings were later reviewed off-line by two judges and rated as to the accuracy of prosodic production. The judges were clinical speech language pathologists (one male, one female) who were familiar with the assessment of prosodic speech disorders. The judges were instructed to evaluate each trial for appropriate use of pitch, rate, and stress, three parameters known to characterize emotional prosody in verbal communication. For instance, happy prosody is typically produced at a fast rate with one or two words dramatically stressed with sentence final rising pitch. However, prosody with negative valence is usually produced with a slower rate of production and limited changes in pitch, with each word harshly stressed.

The judges were instructed to score each subject's in and out of scanner prosodic productions based on the following scoring system utilized to reveal gradations of prosodic accuracy. If the judges assessed that the prosodic production correctly matched the emotional target cue unambiguously (either happy, neutral, or angry prosody) they gave the trial a score of +2. If the prosodic production of that trial closely, but not perfectly, matched the target emotional prosody with less than prototypical levels of pitch, rate, or stress, it was given a score of +1. If the subject's prosodic response did not match the cued emotional prosody, a score of 0 was given.

The two judges independently scored the recorded audiotape of Control Measure 1 performances for all subjects and the ratings of the two judges were then averaged to form a group average for that trial. The averages for each condition (happy, angry, and neutral prosody) for each individual subject were calculated and a prosodically correct percentage was calculated. For example, for the 25 happy trials a score of 50 out of a potential 50 would have been given a 100% prosodically accurate assessment, while a score of 15 out of 25 would have been given a 60% prosodically correct rating. The separate scores determined by the two judges were then compared to each other across all subjects to establish the degree of agreement between these two independent assessments.

Control Measure 2: Subjective Evaluation of Emotional Experience

To monitor the subject's self-perception of emotional experience during the experimental trials in the scanner, each of the subjects were given a written questionnaire (see Appendix B). They were asked questions such as "When you were saying the sentence with happy prosody, did you actually feel happy, or did your voice only sound happy?", or "When you were in the scanner and asked to produce a happy tone in your voice, do you believe it actually sounded happy?".

Experimental Tasks

Along with the required structural MR brain scans, three functional MRI scans (6 minutes and 44s each) were obtained from each subject which were composed of 25 individual 16.17s trials during which the subject overtly produced a single phrase ("They went to the store"). While in the scanner, subjects were able to hear the experimenter from the control console and task demands were briefly reviewed prior to each individual scan. These instructions were provided by the same individual who provided the initial training to ensure consistent performance across subjects.

Two different scanner operators facilitated the technical aspects of the acquisition of the MR signal. During each trial of the functional scans, subjects were presented with a visual cue for the target emotional prosody (angry, happy, or neutral). The presentation of the visual stimuli (see Figure 7) occurred in the initial 2.94s of the trial and the subject responded with the overt production of the target sentence with the cued emotional prosody (happy, angry, or neutral). The stimulus display of 2.94s (2 image epochs) was followed by a blank screen for an interval of 13.23s. Subjects were instructed to lie quietly with their eyes open during this 13.23s period. The visually presented neutral sentence and target prosody (black text on a white background) appeared on a screen that was visible to the subject by a mirror built into the head coil of the scanner. The screen was located fifteen feet from the subject's head and the letters were approximately eight inches in vertical height on that screen. These stimuli were presented via a LCD projector connected to a Dell Latitude XPi laptop running the SuperLab Pro presentation program (Cedrus Inc., Phoenix, AZ).

Therefore, subjects completed three functional scans which were randomly blocked and composed of 25 happy, 25 angry, and 25 neutral trials (16.17s each trial). Each functional scan lasted six minutes and 44s in its entirety.

"They went to the store"

HAPPY

Figure 5. An example of the stimuli presented to subjects during the experiment.

fMRI Scanning Parameters

All studies were completed using a 1.5 Tesla GE Signa with a 2-spiral gradient echo scan (Noll, Cohen, Meyer, and Schneider, 1995) with the following parameters: nine contiguous axial 6.9 mm thick slices (11 images per cycle or 276 total images per run), 180 mm FOV, voxel size = 1.4 x 1.4 x 6.9 mm (initial acquision), TR/TE/FA = 735ms/30ms/40deg, 2.94s per image set, with six initial discarded images (4.41s). High-resolution anatomic images were also obtained with a 3D-SPGR sequence (TR/TE/FA = 27ms/7ms/45deg), FOV = 240 mm, 256 x 256 x 124 matrix, voxel size = 0.94 x 0.94 x 1.3 mm in initial acquisition). A domed quadrature rf head coil was used with foam padding for head stabilization. Prior to the functional images, time of flight MR angiograms were acquired for the same nine axial slices as the functional images.

fMRI Data Analysis

To reduce the effects of head motion, images from each run were first spatially registered in-plane to a base image using an iterative linear least squares approach (Keren, Peleg, & Brada, 1988). The last image of the last functional imaging run was selected as the base image because its acquisition immediately preceded that of the anatomic images used as an underlay for the functional images. To reduce large vessel effects and other potential sources of artifact, voxels whose standard deviation exceeded 5% of the mean signal were set to zero before further processing. The individual time series for each subject was visually inspected for gross artifacts.

Initially a prosody vs. null hypothesis Student t-test comparison was performed on a voxel-by-voxel basis for each of the three conditions (angry, happy, and neutral). A very stringent statistical threshold ($p < 0.000001$) for positive voxels was utilized because of the inherently high statistical power of these initial gross comparisons. It was expected that large volumes of bilateral activity would be revealed for each of these comparisons.

To provide more specific experimental comparisons, a pseudo-event related technique that was used in this study was an adaptation of Birn *et al.* (1999b) technique which was created to permit overt production in a fMRI experiment. Each trial was divided into 11 equal 1.47s epochs in a pseudo-event related technique (see Figure 6). During initial processing, a t-test comparison was performed based on difference between the average MR signal change produced during the 4th and 5th epochs (4.41s to 7.35s) and the average MR signal change created during the last two epochs (from 13.23s to 16.17s). Cohen (1997) noted that the hemodynamic response tends to peak in activated cortical tissue in this four to seven second range. This process thereby omitted from analysis the initial period during which subjects spoke. This technique was utilized because it had the potential of reducing artifactual activation related to movement, thereby more clearly isolating task related activity.

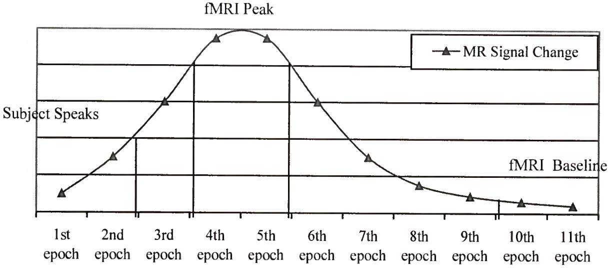


Figure 6. A depiction of a single experimental trial during which the subject sees the visual stimuli and responds during the initial 2 epochs (2.94s), the 4th and 5th epochs which were used as the main basis of comparison (4.41s to 7.75s), once the baseline activation created during the 10th and 11th epochs (13.23s to 16.17s) were subtracted. Therefore, only the fMRI data acquired during the 4th & 5th, and 10th & 11th epochs were actually used in analysis.

The datasets of each individual subject were then evaluated on a voxel-by-voxel basis to compare the functional scans during which emotional prosody was produced with the scans during which neutral prosody was produced. A probability of $p < 0.001$ for positive voxels was selected to provide a stringent threshold for significant brain activity and also to eliminate any possible extraneous artifactual activity. This Student t-test comparison ($p < 0.001$; $n = 25$; $t = 1.003$) utilized the Cornish-Fisher expansion (Fisher & Cornish, 1960) to compensate for the multiple comparisons across the 12 subjects. The averaged *t*-values were used to control for heteroscedasticy of MR signal variation between subjects because of events unrelated to the experimental task demands such as scanner variability between sessions, variability in global blood flow and/or hematocrit, or differing degrees of cardiac effects (Binder *et al.*, 1999).

After pre-processing of each of the subjects' datasets had been completed, all of the structural and functional datasets for each subject were interpolated to 1 mm^3 voxels, co-registered and converted to standard atlas space (Talairach and Tournoux, 1988) through a procedure within the AFNI program. To compensate for individual subject variability in functional anatomy, the functional image volumes were spatially smoothed 3 mm, by replacing each voxel value with the average value of the others within a 3 mm radius. Then the functional datasets were merged across all 12 subjects, by averaging the functional intensity represented by the t statistic for each voxel across all conditions. A clustering program that is a component of the AFNI package was used to tabulate the number of positive voxels (1.0 x 1.0 x 1.0 mm) with a p value less than 0.001 that were located in a contiguous cluster of at least 100 interpolated voxels (> 100 micro liters) in volume. This information was used to evaluate the volume of significant activity for each experimental comparison. These significantly active voxels were visualized through their display over a merged structural image obtained from the individual structural images of the 12 subjects. Brodmann's areas and neuroanatomic gyral regions were determined by a computerized database (Collins, Holmes, Peters, & Evans, 1995) which applied these labels based on the Talairach coordinates (Talairach and Tournoux, 1988) of the most significant voxel within a single cluster of voxels.

Experimental Comparisons

Experimental Comparison 1: Happy vs. Neutral Prosody

If the right hemispheric hypothesis is correct, greater right than left hemispheric engagement should have been present as a result of this comparison. It was hypothesized that the brain activity related to the common motoric and language demands of both tasks, would have been minimized in this process.

Alternatively, if the valence hypothesis is correct, this happy vs. neutral prosody comparison would predict preferential engagement of the left, not the right, hemisphere.

Experimental Comparison 1 would provide the critical information needed to discriminate between these two competing models, because each posited a different pattern of hemispheric lateralization for this comparison.

Experimental Comparison 2: Angry vs. Neutral Prosody

Additionally, for each subject, a comparison was performed between the activity related to the expression of angry prosody and that created during the expression of neutral prosody.

If the right hemispheric hypothesis is correct, a angry vs. neutral comparison should have revealed greater right than left hemispheric engagement. Similarly, the valence hypothesis also predicted that this comparison would have shown preferential engagement of the right hemisphere as a result of this analysis.

Therefore, while Experimental Comparison 2 would provide supporting evidence of the validity of both of these hypotheses, it would not have provided the critical evidence needed to discriminate between these two models which Comparison 1 provided.

Experimental Comparison 3: Angry vs. Happy Prosody

Due to the novelty of the data analysis techniques, two additional comparisons were also performed to better characterize the patterns of activation associated with the other comparisons. However, no *a priori* hypothesis of the results of these comparisons was conjectured, although the results would likely inform the analysis of Experimental Comparisons 1 & 2.

Experimental Comparison 4: Happy vs. Angry Prosody

An additional comparison contrasted the production of happy vs. angry prosody.

CHAPTER 3
RESULTS

Subjects Screening Measures

None of the twelve subjects reported recent signs of depression or a past history of psychiatric illness for themselves or their immediate family as documented in the pre-scan subject checklist (see Appendix 1), and in their responses to the Beck Depression Inventory (1987). Each subject's individual scores as well as the collective average scores for the Beck Depression Inventory (mean of +.75; SD = 1.2) were well below the cut off score of +11 for clinical depression. Therefore it was surmised that the subjects were not actively depressed at the time of testing. The subjects reported no past history of neurological injury, and did not report any history of ADHD or other learning disabilities.

The average age of the 12 subjects was 27.2 (SD = 7.4) years old at the time of testing (see Table 1) and their average educational level was 14.5 (SD = 2.4) years of formal education. The two groups of six men and six women did not differ significantly with respect to age or education.

Table 1. Information concerning subject educational background, age, psychological status, and hand use.

Sex	Age	Ed.[a]	B&N[b]	Waterloo[c]	Beck[d]
M	24	16	23	68	0
M	20	16	21	67	0
F	24	18	22	72	3
F	19	14	24	65	0
M	21	16	22	65	2
F	18	12	21	64	1
F	27	16	20	67	3
F	21	12	21	66	0
F	32	18	24	69	0
M	31	16	24	65	0
M	42	18	24	72	0
M	28	16	23	60	0

[a] Educational level

[b] Briggs & Nebes Handedness Inventory

[c] Waterloo Handedness Questionnaire - Revised

[d] Beck Depression Inventory

All 12 subjects were strongly right handed as supported by their performance on the Waterloo Handedness Questionnaire (Steenhuis and Bryden, 1989) which revealed a mean of 67 (SD = 3.3) out of a possible 72 representing a strong right hand bias. Subjects also demonstrated a mean of 22 (SD = 1.4) out of a possible 24 on the Briggs & Nebes (1987) handedness inventory, which also placed them within a strongly right handed designation.

Control Measures

Control Measure 1: Prosody Production Within and Outside of Scanner

This control measure was designed to rule out the possibility that subjects were simply distracted by the loud, confining environment of the scanner, which may have induced anxiety thereby limiting the extent to which they could have felt and sounded happy. The judges assessed the prosodic accuracy of the subject's responses during experimental testing within the MR scanner environment (+2 accurate, +1 closely matched target, 0 no match to target prosody). The averages for each condition (happy, angry and neutral) for each individual subject were calculated and a prosodically correct percentage was calculated.

Additionally, Control Measure 1 was performed to ensure that even if the loud acoustic background noise of the scanner precluded recording the subject's voice in the scanner, the subject's renditions of emotional prosody could be evaluated from recordings made outside the scanner environment that same day.

As noted in Table 2 it was not possible to assess the in-scanner verbal production for subjects s01 and s02 due to an unexpected technical problem. It was observed that when audio-recording was attempted from a tape recorder that was plugged into a electric wall receptacle for power, the recording was unintelligible because of a RF carrier noise offset. In essence, the microphone cord acted as a antenna and re-broadcast a harmonic of the original RF pulse thereby disrupting the audio-recording. Proper grounding of the electric receptacles in the MR console room would have eliminated this carrier noise. This problem was eliminated in later experimental trials by operating the tape recorder from battery power. Overall the use of a bi-directional microphone appeared to be effective and it partially cancelled the very loud background noise produced by the MRI scanner. The judges noted that while a number of subjects utilized a low speaking volume during the experimental trials, it was still possible to hear their production on the audiotape, above the background noise of the scanner.

The prosodic accuracy scores for the 12 subjects in the study are depicted in Table 2 with group comparisons depicted in Table 3. Almost without exception, subjects produced neutral prosody with 100% accuracy both within and outside of the scanner environment. Additionally, the overall average for all 12 subjects revealed comparable levels of prosodic accuracy for both emotional prosodies inside and outside the MRI scanner environment. For instance, during the production of happy prosody the overall average for all 12 subjects was 80% inside, compared to 75% outside. During the production of angry prosody inside the scanner the overall average for all 12 subjects was rated to be 62% prosodically accurate, while outside it was rated to be 68% accurate. These figures also reveal the differential accuracy for each emotional prosody, with higher accuracy ratings for the production of happy prosody, than for angry prosody. The grouped comparisons depicted in Table 3 (2 tailed t-test, $p < 0.05$) revealed no significant difference between in-scanner vs. out of scanner prosodic accuracy within each of the three emotional prosodies (e.g., Angry-In vs. Angry-Out). However, there were significant differences (see Table 3) when the scanner condition (e.g., In or Out) was held constant and comparisons were made across each of the three emotional prosodies. The only exception to this was the Angry-Out vs. Happy-Out comparison revealed a trend, but did not reach significance at $p < .06$.

These findings support the hypothesis that subjects were not distracted by the loud, potentially anxiety provoking environment of the scanner, and produced a comparable level of prosodic accuracy whether they were within or outside the scanner. The agreement between the two judges for this control measure across the available 10 subjects was greater than 96% for the trials within, as well as outside the scanner.

Control Measure 2: Subjective Evaluation of Emotional Experience

This control measure was designed to assess the possibility that subjects had actually experienced an emotion other than the target emotion during the experimental trials, even when their prosodic production matched the target prosody. Therefore Control Measure 2 provided subjects with a questionnaire which was filled out after the scan to probe their subjective perception of their prosodic production. They were asked to write answers to questions such as "When you were saying the sentence with happy prosody, did you actually feel happy, or did your voice only sound happy?".

The subjects' responses to this post-scan subjective evaluation of emotional experience revealed a presumed match of target prosody to emotional experience of 100% for neutral and happy trials (12 out of 12 subjects). Eleven out of the 12 subjects reported that during their production of angry prosody they actually felt angry, while one subject reported that they did not feel angry during the production of angry prosody. Thus in general the subjects stated that their emotional state at the time of the verbal prosodic production in the scanner matched the target emotional prosody they were producing.

Experimental Comparisons

A small artifact was noted to occur in the images due to a radio frequency carrier noise offset or a DC signal artifact. This was likely caused by the presence of the ungrounded microphone cord in the MR scanning room. During experimental trials the scanner door was left slightly ajar to permit the microphone cord to pass through. This also could have contributed to this artifact. This "zipper" (Kruggel, von Cramon, & Descombes, 1999; Haacke, Brown, Thompson, & Venkatesan, 1999) artifact occurred across phase encoding and did not appear to induce distortions of the datasets.

Initial Processing

A prosody vs. null hypothesis Student t-test comparison was performed voxel-by-voxel for each of the three conditions. A very stringent statistical threshold ($p < 0.000001$) for positive voxels was utilized because of the inherently high statistical power of these initial gross comparisons. Large volumes of significant clusters (>500 μL) were revealed bilaterally for each of the three comparisons (see Figures 7-10). For instance, the happy prosody vs. null comparison (see Table 4 and Figure 8) revealed a large volume of activity in the right precentral gyrus and precuneus region, with a smaller volume of activity noted to occur in the left precentral gyrus and insula, as well as the right superior temporal and postcentral gyrus, and the right caudate region. The angry prosody vs. null hypothesis comparison (see Table 5 and Figure 9) revealed a similar pattern of activity with a large volume in the precentral gyrus bilaterally ($R > L$), with lesser amounts in the right superior frontal, inferior parietal, precuneus and postcentral gyrus. The neutral prosody vs. null hypothesis comparison (see Table 6 and Figure 7) revealed a large volume of activity in the right precentral gyrus, and lesser amounts in the left precentral gyrus, right superior frontal gyrus. It is noteworthy that while right precuneus activity was noted to occur medially in the two emotionally related comparisons (angry and happy), this was not noted to occur in the neutral prosody vs. null hypothesis comparison (see Figure 10).

To provide more specific experimental comparisons, voxel-by-voxel Student t-test ($p < 0.001$) contrasts were performed between the functional MR datasets related to the expression of emotional prosody and those created during the expression of neutral prosody for all subjects. In contrast to the initial prosody vs.

null hypothesis comparisons, this technique was utilized because it had the potential of reducing artifactual brain activity related to head movement by eliminating from analysis the initial 4.41s during which the stimulus was presented and speech was produced, thereby more clearly isolating task related activity.

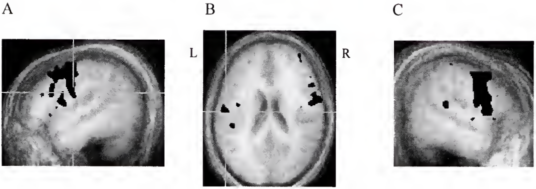


Figure 7. Significant ($p < 0.00001$) activity was noted to occur bilaterally as a result of a neutral prosody vs. null hypothesis comparison averaged across all 12 subjects. These large significant clusters (> 500 μL) were displayed in images from the left para-sagittal plane (A), a matching axial (B) image, and a para-sagittal image (C) from the right hemisphere.

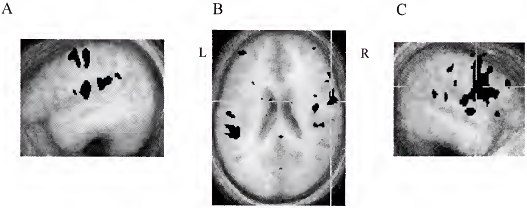


Figure 8. Significant ($p < 0.00001$) activity was noted to occur bilaterally as a result of a happy prosody vs. null hypothesis comparison averaged across all 12 subjects. These large significant clusters (> 500 μL) were displayed in images from the left para-sagittal plane (A), a axial (B) image, with a matching para-sagittal image (C) from the right hemisphere.

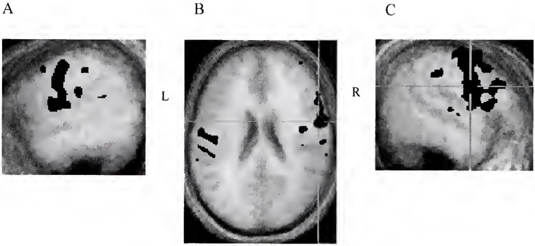


Figure 9. Significant ($p < 0.00001$) activity was noted to occur bilaterally as a result of a angry prosody vs. null hypothesis comparison averaged across all 12 subjects. These large significant clusters (> 500 μL) were displayed in images from the left para-sagittal plane (A), a axial (B) image, with a matching para-sagittal image (C) from the right hemisphere.

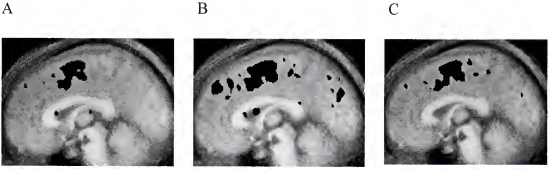


Figure 10. Significant ($p < 0.00001$) activity was noted to occur medially as a result of the prosody vs. null hypothesis comparisons averaged across all 12 subjects. These significant clusters (> 500 μL) were displayed in the mid-sagittal plane for the following comparisons: (A) neutral prosody vs. null hypothesis, the (B) happy prosody vs. null hypothesis, and the (C) angry prosody vs. null hypothesis.

Experimental Comparison 1: Happy vs. Neutral Prosody

As depicted in Table 7, the significant brain activity based on averaged data for all 12 subjects demonstrated only a single volume of activity in the right hemisphere. It is noteworthy that no activity was revealed in the traditionally defined language cortices of the left hemisphere, even though this was a language production task. This area of activity were limited in volume and was confined to the precentral gyrus of the right hemisphere (see Figure 11).

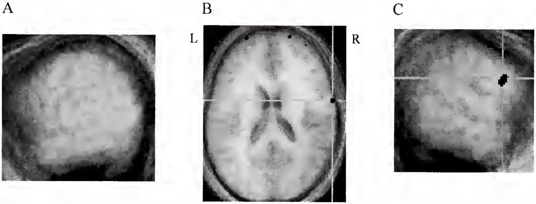


Figure 11. Significant ($p < 0.001$) activity was noted to occur in the right precentral gyrus as a result of a t-test comparison between the production of happy vs. neutral prosody averaged across all 12 subjects. No activity was present in the para-sagittal image (A) from the left hemisphere, but a significant cluster (> 100 μL) was present in the right hemisphere as depicted in the axial plane (B), and the matching para-sagittal image (C).

Experimental Comparison 2: Angry vs. Neutral Prosody

As depicted in Table 8, the significant brain activity averaged across all 12 subjects demonstrated exclusive engagement of the right hemisphere without any left hemisphere engagement. The strongest areas of activity were in the right superior and middle frontal gyrus (see Figures 12 and 13), with additional areas of activity in the right posterior cingulate (see Figure 14), and the right angular gyrus (see Figure 15). Again it is noteworthy that no activity was revealed in left hemisphere, even though this was a language production task.

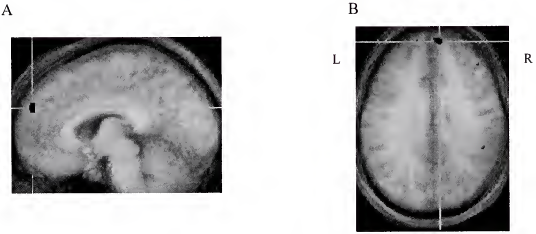


Figure 12. Significant ($p < 0.001$) activity was noted to occur in the right superior frontal gyrus as a result of a t-test comparison which contrasted the production of angry vs. neutral prosody averaged across all 12 subjects. This significant cluster ($> 100\ \mu L$) was displayed in the sagittal (A) and matching axial (B) plane.

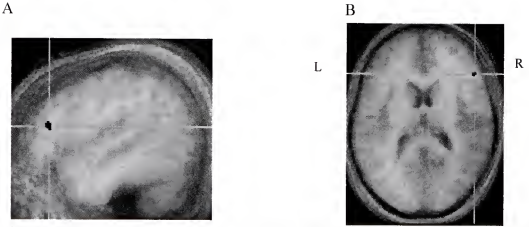


Figure 13. Significant ($p < 0.001$) activity was noted to occur in the right middle frontal gyrus as a result of a t-test comparison between the production of angry vs. neutral prosody across all 12 subjects. This significant cluster (> 100 μL) was displayed in the sagittal (A) and matching axial plane (B).

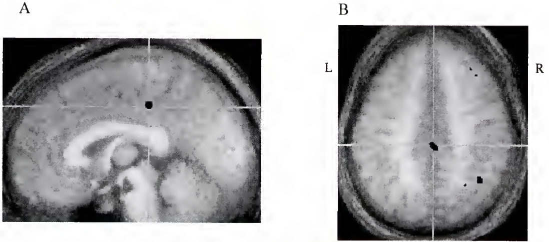


Figure 14. Significant ($p < 0.001$) activity was noted to occur in the right posterior cingulate cortex as a result of a t-test comparison between the production of angry vs. neutral prosody averaged across all 12 subjects. This significant cluster (> 100 μL) was displayed in the sagittal (A) and axial (B) planes.

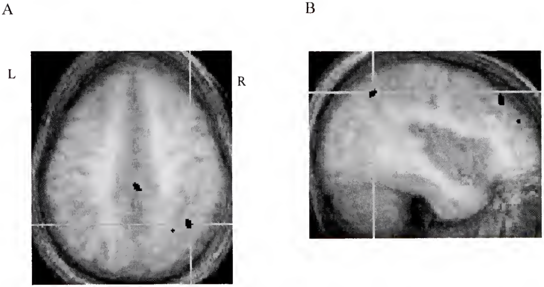


Figure 15. Significant ($p < 0.001$) activity was noted to occur in the right angular gyrus as a result of a t-test comparison between the production of angry vs. neutral prosody averaged across all 12 subjects. This significant cluster (> 100 µL) was displayed in the (A) axial and (B) sagittal planes.

Experimental Comparison 3: Angry vs. Happy Prosody This comparison did not reveal any significant areas of activation.

Experimental Comparison 4: Happy vs. Angry Prosody This final comparison contrasted the production of happy prosody contrasted with negative valence (see Table 8). This comparison revealed wide ranging activity including the only cluster of left frontal gyrus activity among all fourof the comparisons. Engagement of the left hemisphere was extensive at a volume of 771 µL, but right hemisphere volume was still greater at a volume of 1354 µL. The greatest regions of activity were noted to occur in the right insula, angular gyrus, and the right superior parietal lobule. More limited volumes of activity also occurred in the right superior frontal gyrus and the posterior cingulate. Activity in the left hemisphere was revealed in the parietal precuneus, SMA, and the left insula.

Summary of Results

Control Measures

Based on the results of Control Measure 1, which depicted comparable ratings both within and outside the MRI scanner for the prosodic accuracy for all 12 subjects, it was concluded that the subjects were not distracted by the loud environment of the scanner. Furthermore, this provided evidence that the confining setting inside the magnet did not induce anxiety, which could have limited the extent to which subjects expressed the target emotional prosodies. Furthermore, the results of the subjective questionnaires which subjects completed as part of Control Measure 2 provided support for the hypothesis that during the experimental trials the subjects may have actually experienced the target emotion associated with the cued prosody.

Research Question 1

The initial gross prosody vs. null hypothesis analysis revealed large bilateral (R > L) areas of activity across all three comparisons, most prominently in motorically related cortices such as the prefrontal, and superior frontal gyri (see Table 10). It is noteworthy that Table 10 did reveal extensive differences in the volumes of the prosody vs. null hypothesis comparisons. For example, the happy vs. null hypothesis comparison was approximately 25% larger in volume than the angry vs. null hypothesis, and was approximately 50% larger than the neutral vs. null hypothesis comparison. This variability may have induced a degree of error in the comparisons. For instance, this large difference in volume between angry or happy, may have skewed the results when each was compared to the fairly limited volumes associated with neutral prosody.

Because Experimental Comparisons 1 & 2 did not reveal activity in known language cortices such as the left inferior gyrus, this suggests that this pseudo-event related technique effectively minimized the fMRI activity related to the common language and motoric aspects of speech production. Table 6 demonstrates that only the right precentral region was activated as a result of the happy vs. neutral prosody comparison. While the volume of this activated region was limited, this motorically related region did reach the stringent statistical threshold set for this comparison (see Figure 11). Finally, Table 7 depicts the angry vs. neutral prosody results, which revealed exclusive right hemisphere activity (see Figure 12-13) as a result of this comparison.

While it is problematic to evaluate the findings of the final two comparisons (Experimental Comparisons 3 & 4), they too revealed greater right than left hemisphere activity. Each of these depict the brain regions that were required to produce a particular emotional prosody, over and above the activity required to produce the other emotional prosody. For instance, no significant activity was revealed for the angry vs. happy prosody comparison. Yet, the results of the happy vs. angry prosody comparison (Table 8), reveals strong right hemisphere activity, with only limited left hemisphere activity.

Research Question 2

As depicted in Tables 4-6 all three gross comparisons of overt speech production vs. null hypothesis induced greater right than left hemisphere activity with the largest clusters located in the right frontal region (Table 10). In both the happy vs. neutral (Table 8) and the angry vs. neutral prosody (Table 7) comparisons the largest clusters were again located in the right frontal region (Table 10).

Table 2. In-scanner vs. out-of-scanner prosodic accuracy as determined by two raters for all 12 subjects.

	Emotional Prosody					
	Happy		Angry		Neutral	
	In[a]	Out[b]	In[a]	Out[b]	In[a]	Out[b]
	NA[c]	NA[c]	NA[c]	NA[c]	NA[c]	NA[c]
	NA[c]	NA[c]	NA[c]	NA[c]	NA[c]	NA[c]
	32/64%	8/67%	30/60%	7.5/63%	50/100%	12/100%
	30/60%	7/58%	27/54%	4.5/38%	50/100%	12/100%
	50/100%	12/100%	48/96%	11.5/96%	50/100%	12/100%
	33.5/67%	9.5/79%	41/82%	10.5/88%	50/100%	11.5/96%
	40.5/81%	9/75%	18.5/37%	6.5/54%	50/100%	12/100%
	38/76%	8/67%	26/52%	7.5/63%	50/100%	12/100%
	44/88%	10/83%	27/54%	9/75%	50/100%	12/100%
	48.5/97%	11.5/96%	45/90%	10.5/88%	50/100%	12/100%
	49/98%	5/83%	20/40%	5.5/46%	50/100%	12/100%
	37/74%	9.5/79%	27/54%	9/75%	50/100%	12/100%
M	40/80%	8.95/75%	31/62%	8.2/68%	50/100%	11.95/99%
SD	7.4	2.1	10.2	2.3	0.0	0.2

[a] In-scanner trials composed of 25 trials for each emotional prosody. Percentage is based on 25 trials with a maximum possible score of 50 (2 = accurate prosody, 1 = close to target prosody, 0 = incorrect prosody).

[b] Out-of-scanner trials were composed of 6 trials for each emotional prosody. Percentage is based on 6 trials with a maximum possible score of 12 (2 = accurate prosody, 1 = close to target prosody, 0 = incorrect prosody).

[c] Due to a technical problem the in-scanner prosody was not able to be recorded.

Table 3. T-test comparisons ($p < 0.05$) between in-scanner vs. out-of-scanner prosodic accuracy as determined by two raters for all 12 subjects.

Comparisons	Significance Level
Angry-In vs. Angry-Out	.098
Happy-In vs. Happy-Out	.472
Neutral-In vs. Neutral-Out	.343
Angry-In vs. Happy-In	.025*
Angry-In vs. Neutral-In	.001*
Happy-In vs. Neutral-In	.002*
Angry-Out vs. Neutral-Out	.001*
Happy-Out vs. Neutral-Out	.001*
Angry-Out vs. Happy-Out	.062

* $p < 0.05$

Table 4. Volume (μL) of significant ($p < 0.00001$) fMRI clusters (> 500 μL) as a result of a happy prosody vs. null hypothesis t-test comparison averaged across all 12 subjects.

BA[a]	Region	Talairach Coordinates			Volume/μL
		x	*y*	*z*	
6	R precentral gyrus	51.0	-1.0	40.0	15158
6	R precentral gyrus/SMA[b]	0.0	6.0	54.0	11373
7	R parietal precuneus	13.0	-68.0	34.0	4114
9	R precentral gyrus	-44.0	-18.0	39.0	4043
13	L insula	-48.0	-29.0	20.0	1686
6	L precentral gyrus	-53.0	-6.0	9.0	1680
	R caudate/white matter	6.0	7.0	14.0	1174
7	R postcentral gyrus	10.0	-46.0	61.0	999
42	R superior temporal gyrus	57.0	-31.0	12.0	704
	R caudate/white matter	8.0	19.0	10.0	646
4	R precentral gyrus	35.0	-27.0	55.0	577

[a] BA = Brodmann's area

[b] SMA = supplemental motor area

Table 5. Volume (μL) of significant ($p < 0.00001$) fMRI clusters (> 500 μL) as a result of a angry prosody vs. null hypothesis t-test comparison averaged across all 12 subjects.

BA[a]	Region	Talairach Coordinates			Volume/μL
		x	*y*	*z*	
6	R precentral gyrus	53.0	-2.0	38.0	12531
4	L precentral gyrus	-43.0	-17.0	37.0	9026
6	R superior frontal gyrus	2.0	6.0	54.0	6607
40	R inferior parietal lobule	62.0	-29.0	26.0	1343
7	R parietal precuneus	19.0	-67.0	48.0	1328
7	R postcentral gyrus	28.0	-23.0	61.0	549
7	R postcentral gyrus	10.0	-48.0	61.0	530

[a] BA = Brodmann's area

Table 6. Volume (μL) of significant ($p < 0.00001$) fMRI clusters (> 500 μL) as a result of a neutral prosody vs. null hypothesis t-test comparison averaged across all 12 subjects.

BA[a]	Region	Talairach Coordinates			Volume/μL
		x	*y*	*z*	
6	R precentral gyrus	52.0	-3.0	26.0	10866
4	L precentral gyrus	-48.0	-16.0	44.0	5620
6	R superior frontal gyrus/SMA[b]	2.0	6.0	53.0	5187
8	R superior frontal gyrus	30.0	43.0	39.0	662

[a] BA = Brodmann's area

[b] SMA = supplemental motor area

Table 7. Experimental Comparison 1: volume (μL) of significant ($p < 0.001$) fMRI clusters (> 100 μL) as a result of a happy vs. neutral prosody t-test comparison averaged across all 12 subjects.

BA[a]	Region	Talairach Coordinates			Volume/μL
		x	*y*	*z*	
4	R precentral gyrus	61.0	0.0	20.0	173

[a] BA = Brodmann's area

Table 8. Experimental Comparison 2: volume (μL) of significant ($p < 0.001$) fMRI clusters (> 100 μL) as a result of a angry vs. neutral prosody t-test comparison averaged across all 12 subjects.

BA[a]	Region	Talairach Coordinates			Volume/μL
		x	*y*	*z*	
9	R superior frontal gyrus	6.0	54.0	27.0	283
9	R middle frontal gyrus	37.0	32.0	35.0	151
31	R posterior cingulate	1.0	-28.0	41.0	121
39	R angular gyrus	42.0	-43.0	24.0	117

[a] BA = Brodmann's area

Table 9. Experimental Comparison 4: volume (μL) of significant ($p < 0.001$) fMRI clusters (> 100 μL) as a result of a happy vs. angry prosody t-test comparison averaged across all 12 subjects.

BA[a]	Region	Talairach Coordinates			Volume/μL
		x	*y*	*z*	
13	R insula	46.0	-14.0	11.0	397
39	R angular gyrus	-30.0	-38.0	36.0	365
7	R superior parietal lobule	27.0	-55.0	43.0	269
7	L parietal precuneus	-5.0	-61.0	45.0	225
7	L parietal precuneus	-16.0	-60.0	45.0	217
6	R superior frontal gyrus	16.0	18.0	52.0	210
6	L SMA[b]	-4.0	8.0	47.0	177
13	L insula	-46.0	-35.0	22.0	152
31	R posterior cingulate	1.0	-27.0	42.0	113

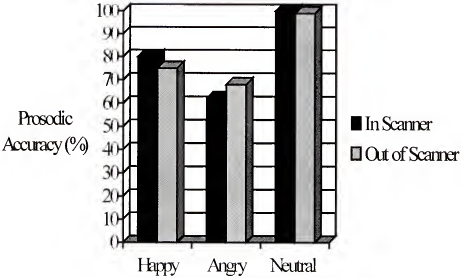
[a] BA = Brodmann's area

[b] SMA = supplemental motor area

Table 10. Overall volume (μL) of hemispheric activity associated with all comparisons, averaged across all 12 subjects.

Comparison	Hemisphere		Frontal Lobe	
	Left	Right	Left	Right
Happy vs. Null Hypothesis	3,366	38,788	1,680	31,151
Angry vs. Null Hypothesis	9,026	22,888	9,026	19,138
Neutral vs. Null Hypothesis	5,620	16,715	5,620	16,715
Happy vs. Neutral Prosody	0	173	0	173
Angry vs. Neutral Prosody	0	672	0	434
Happy vs. Angry Prosody	771	1,354	329	607
Angry vs. Happy Prosody	0	0	0	0

Figure 16. In-scanner vs. out-of-scanner prosodic accuracy as determined by two raters for all 12 subjects.



CHAPTER 4
DISCUSSION

Introduction

The purpose of this study was to test whether the production of emotional prosody was lateralized. The right hemisphere dominance hypothesis posited that greater brain activity would be present in the right hemisphere regardless of the valence of the emotional prosody. Alternatively the valence hypothesis posited that the brain activity would be greater in the left hemisphere during the production of positive prosody and greater in the right during the production of negative prosody. These competing hypotheses were evaluated with fMRI which provided the localization and volume of brain activity related to the production of a neutral declarative sentence (e.g., “They went to the store”) intoned with either happy, angry, or neutral prosody.

Research Question 1

Does the experimental evidence support the validity of the right hemisphere dominance hypothesis, the valence hypothesis, or a third alternative?

A priori Prediction

It was predicted that this fMRI experiment would provide greater support for the right hemisphere dominance hypothesis when the production of emotional prosody was compared to neutral prosody production.

The findings of the happy vs. neutral prosody comparison revealed only a single area of activity in the right premotor area, while the angry vs. neutral comparison revealed significant activity in the right middle frontal gyrus and prefrontal regions, the right posterior cingulate, and the right angular gyrus. A number of issues should be resolved prior to addressing Research Question 1. For instance, why was there a difference in the perceptual ratings of the prosodic accuracy of the subjects between the production of angry and happy utterances? Was there a fundamental difference in the acoustic profile between the production of happy or angry prosody? Was it appropriate to use neutral prosody as a baseline for either angry or happy prosody? Is there a fundamental difference in the degree to which the expression of either happy or angry prosody requires an internal emotional response or experience? Did the subjects actually experience happiness or anger during task performance? Finally, why is the happy vs. neutral prosody comparison so limited in volume, in reference to the angry vs. neutral contrast?

Why the Difference in the Ratings of Angry and Happy Prosody?

The accuracy of the in-scanner happy prosodic utterances (Table 16) were judged to be more accurate (80% accuracy), than the angry prosodic productions (62% accuracy). Pell (1999b) reported strikingly similar findings when judges assessed the prosody productions of normal controls which revealed that they were more proficient in transmitting happy prosody (78% accuracy) than they were in communicating angry prosody (64% accuracy). Therefore, the difference in the ratings of happy and angry prosody appears to be a robust and reliable measurement. However, it is not known why a difference between these two prosodic utterances would exist.

Differences in the Acoustic Profiles of Angry and Happy Prosody?

This was not quantified in this present study. However, if a different acoustic profile was associated with each emotional prosody, this could account for the mismatch in the perceptual ratings between angry and happy prosody. One prosody may be easier to identify than another. Pell (1999a) demonstrated that the rate of production of happy prosody (4.68 words per second) was more similar to the rate for neutral (4.97 words per second) prosody, than it was to the production of angry prosody (4.01 words per second). In a study of the acoustic parameters of emotional prosody Pell (1999b) revealed that normal control subjects produce happy utterances with an elevated mean fundamental frequency (F_0) with a significant rise in F_0 when marking focus on sentence-final items. Neutral utterances were characterized by a less intense version of this pattern with a relatively low mean F_0 and an intermediate amount of F_0 variation. In contrast, the acoustic pattern associated with the production of angry prosody demonstrated a more uniform F_0 level. Pell (1999b) noted a significantly higher mean F_0 when happy was compared to angry (final focus). Therefore, happy prosody is acoustically more similar to neutral prosody, then it is to angry prosody. It is unknown if these acoustic similarities would be related with a correspondingly similar pattern of brain activity. If these brain patterns were similar, this could have minimized the significant areas of activity that would have been revealed when happy was compared to neutral prosody, consistent with the findings of this dissertation.

Was it Appropriate to Utilize Neutral as a Baseline for Emotional Prosody?

An unexamined *a priori* assumption was that neutral prosody had a minimal amount of intonation and was a suitable measure to use as a baseline to examine the activity associated with emotional prosodies. However, the neutral vs. null hypothesis comparison revealed an extensive degree of left and right hemisphere activity. This brain activity is likely related to the respective linguistic and prosodic aspects of the task. Additionally, Pell's (1999b) acoustic study of normal controls revealed an intermediate level of F_0 variability during neutral prosody production, not a total lack of variability. As noted earlier, many have argued that neutral prosody operates as a functional baseline along a prosodic continuum which is modified through subtle or more robust inflections to express various emotions (Grandour, Larsen, Dechongkit, Ponglorpisit, & Khunadorn, 1995; Ladd, 1980; Liberman, 1967). Yet, while neutral prosody can be thought of as a functional baseline for emotional prosodies, at the level of brain activity it still requires substantial cortical resources to support this function. It would appear then that neutral prosody is a sub-optimal baseline for comparisons of the brain activity associated with either happy or angry prosody. A more accurate baseline would have been established by the utilization of a utterance which lacked speech prosody (i.e., monotonic or robotic-like voice).

Differences in the Emotional Experience Associated with Happy or Angry?

It is known that it is more socially acceptable to display happy rather than angry emotions. Therefore, the production of happy prosody may be more practiced and as a result could be more automatically generated. For example, to produce a believable rendition of happy prosody might simply require the utilization of a distinct pattern of pitch alterations such as the rise in F_0 on sentence-final items that Pell (1999b) revealed, possibly without an internal experience of happiness. In contrast, projecting a credible angry tone of voice might require more subtle adjustments to vocal quality which are possible only after that emotion has been internally experienced. However, it is difficult to objectively determine whether this hypothesis is correct.

Yet, if a difference does exist at this level, it would then be problematic to make direct comparisons between these two emotional prosodies. Table 10 does reveal extensive differences in the volumes of the prosody vs. null hypothesis comparisons. For example, the happy vs. null hypothesis comparison was approximately 25% larger in volume of activity than the angry vs. null hypothesis comparison, and twice as large as the neutral vs. null hypothesis comparison. These findings suggest that it was problematic to attempt a direct comparison between these two prosodies because of these differences in volume. This then would explain the lack of any significant activity as a result of the angry vs. happy comparison.

Therefore, these empirical differences in brain activity revealed in the happy vs. null and the angry vs. null hypothesis comparisons might possibly represent a variable internal emotional experience associated with either emotional prosody.

Did the Subjects Actually Feel Happy in the Scanner?

Another possibility is that while subjects were judged to sound happy, and they reported that they were happy in the post scan questionnaire, they might not actually have felt happy. If correct, this would have limited their internal emotional experience of happiness and then altered the brain activity associated with this task in unpredictable ways. No objective assessment is available that could accurately determine whether the subjects actually experienced happiness during the experimental trials. The scanner environment is confining, and potentially anxiety-provoking, and could have been a strong deterrent to the subjects experiencing a happy emotion. If this conjecture is correct, during the happy trials of this experiment one could propose that the subjects were in essence attempting to express an emotion they did not truly feel. Having committed themselves to this experiment they may have adopted the Meisner Technique (Meisner and Longwell, 1987) and acted the part. That is, they applied additional flux to their vocal intonation to produce the target happy prosody, while the fMRI results revealed only engagement of motoric cortices.

During the production of angry prosody, it is possible that some of the subjects were experiencing a degree of anxiety during the experimental trials. Anger and anxiety are different emotions, but each are known to facilitate a fight or flight response. It is likely that anger and anxiety are more similar to each other, than they are to happy. For instance, anger and anxiety have been more associated with preparation for action, in contrast to happy which may be more passive and evaluative (Heilman, 1994). Adopting Stanislawsky's (1936) acting technique known as The Method (see also Strasberg, 1987), during the scan this fight or flight arousal might have accentuated the brain activity during the angry trials. This is an interesting speculation, yet the happy vs. null hypothesis comparison was approximately 25% larger in volume when compared to the angry vs. null hypothesis comparison and demonstrated robust activity in both hemispheres. Therefore, these findings argue against the possibility that subjects failed to experience happiness during those trials.

Why was the Happy vs. Neutral Comparison so Limited in Activation?

This is a complex matter, but an integration of the preceding discussion can help to address this issue. It was demonstrated that there was a significant difference between the ratings of angry and happy prosody utterances, likely due to different acoustical profiles associated with each prosody. It was also concluded that it was misleading to utilize neutral prosody as a baseline measure because of its acoustic similarity to happy. This may have lead to a reduced amount of brain activity revealed in the happy vs. neutral comparison. Finally, it appeared that expressing happy prosody is likely associated with a somewhat less intense emotional experience than is angry prosody. While this may have reduced the volume of significant activity in the happy vs. neutral comparison to an extent, it was suggested that the greatest amount of error was induced through the use of neutral prosody as a baseline.

These findings do not invalidate this dissertation, but they do provide a more detailed perspective from which to finally address Research Question 1.

Conclusion - Research Question 1

Therefore, based on the findings of this study, greater support was found for the right hemisphere dominance hypothesis. It is important to note that while these findings raise doubt about the validity of the valence hypothesis, they cannot entirely refute that hypothesis. The crucial comparison for this evaluation was the happy vs. neutral comparison which showed greater right than left hemisphere activity, inconsistent with the valence hypothesis which predicted the opposite lateralization pattern. Yet, because of the questions regarding the appropriateness of the utilization of neutral prosody as a baseline and the paucity of the activity in the happy vs. neutral comparison, this stronger claim can not be fully supported.

Yet, if the right hemisphere dominance hypothesis more accurately represents the brain dynamics associated with the production of emotion, one must still address why other neuroimaging studies (Canli *et al.*, 1998; Imaizumi *et al.*, 1997; Irwin *et al.*, 1997; Paradiso *et al.*, 1997; Sackeim *et al.*, 1982; Sutton *et al.*, 1997) have demonstrated left frontal activity during experiments which involved positive valence. This is highly speculative, but the source of this activity might be related to the utilization of a specific cognitive strategy. That is, during task performance the subjects might have been acting to permit them to outwardly express an emotion which they did not truly feel, thereby engaging left frontal resources in the process. As opposed to The Method (Stanislavsky, 1936) which encourages performers to re-experience an emotional experience from their past, the more pragmatic Meisner acting technique (Meisner & Longwell, 1987) may engage left frontal networks to facilitate an optimal performance.

Research Question 2

Is there any evidence for the existence of a prosodic output module in the right frontal lobe and can a cognitive model of prosody production be generated from this information?

A priori Prediction

It was predicted that the results of this experiment would reveal activity in the right frontal lobe during the production of emotional prosody which would provide tentative evidence for this hypothesized prosodic output module. It was assumed that only limited evidence would be revealed which would support a cognitive model of prosody production.

A number of issues must be resolved prior to addressing Research Question 2. Because of the potential confounds associated with the happy vs. neutral comparison addressed in the preceding section, this discussion will focus on the angry vs. neutral comparison. For instance, this analysis revealed significant activity in the right prefrontal lobe, the right middle frontal gyrus, the right posterior cingulate, and the right angular gyrus. Yet, why would the right frontal lobe be involved in the production of emotional prosody at all? What is the potential role of the right prefrontal region in this process? Do prosodic production and comprehension engage the same brain regions? What is the significance of the right posterior cingulate in prosodic production? Finally, why would the right angular gyrus activate during this task and what possible role would it have in a hypothetical cognitive model of the production of angry prosody?

Why would the Right Frontal Lobe be involved in Prosody Production?

It is logical to presume that prosodic processing would be facilitated by the right hemisphere due to its preferential role in attentional monitoring of the environment (Heilman and van Den Abell, 1980). Lindfield, Wingfield, and Goodglass, 1999) demonstrated that emotional prosody boosts comprehension of lexical elements. It is possible that the undulating alterations in $F_{0,}$ which partially represent emotional prosody, might be used as an acoustic signal to maintain the listeners attention. During development while the left frontal region becomes organized to produce the finely resolved sequences of phonemes utilized in expressive language, it is possible that the right frontal lobe becomes optimized for the coordination of sequential events which help facilitate the attentional goals and processes of the right hemisphere.

Concerning the active regions that have a known role in motor function, the happy vs. neutral prosody comparison revealed activity in the right precentral gyrus, while the angry vs. neutral comparison showed only activity in the right middle frontal gyrus. Why would this difference occur? As noted earlier, there are indications that during speech production Broca's area (Brodmann's areas 44 & 45) is engaged, but it does so in conjunction with associated premotor and primary motor cortex regions (Wildgrubber, Ackermann, Klose, Kardatzki, & Grodd, 1996). It is possible that the greater alterations in F_0 that are associated with the production of happy, as opposed to angry prosody, require more premotor cortical engagement to facilitate the changes in oral and lingual musculature which support this process.

One could propose that the right inferior frontal region might actually coordinate the on-line integration of the suprasegmental F_0 alterations associated with emotional prosody into the acoustic speech stream via cross callosal connections (Ross, Harney, deLacoste-Utamsing, & Purdy, 1981). Watson and Heilman (1983) did report a deficit in repeating affective tone after callosal disconnection had occurred. Additionally, Speedie, Coslett, and Heilman, (1984) studied two patients with mixed transcortical aphasia after left hemisphere lesions. They found that the patients were unable to repeat affective prosody, yet had intact propositional speech. This suggests that the isolated left perisylvian region responsible for propositional speech does not mediate prosody. Speedie *et al.* (1984) posited that this information was normally transferred to the left hemisphere from right hemisphere resources via the corpus callosum. Finally, Klouda, Robin, Graff-Radford, and Cooper (1988) provided acoustical evidence of a specific deficit in prosody production following callosal damage. Klouda and colleagues (1988) described disruptions in F_0 contours in their patient which paralleled the acoustic deficits which have been reported for right hemisphere patients (Pell, 1999b). The intimate neuronal connections between the right frontal region potentially facilitating prosody and the left frontal region orchestrating syntactical generation would support such a hypothesis.

Specifically, why did Prosody Production activate the Right Prefrontal Region?

It is possible that the engagement of this right prefrontal region is simply related to some motoric aspect of facilitating the intonational shifts in F_0 during speech production discussed earlier. The prefrontal regions do receive substantial projections from motorically related cortices. However, many lines of inquiry support the view that the engagement of the prefrontal region during these tasks appears to be related to higher order aspects of cognition, rather than the execution of simple motoric sequences.

The finding of significant activity near the right frontal pole during the production of angry emotional prosody could suggest that emotional prosodic semantics may be supported by this region. To produce an angry tone of voice the subjects would need to access a representation of the acoustic pattern of this prosody based on the visually presented cue. Both frontal poles are known to receive strong projections from the limbic cortex and these frontal regions have a well established, but poorly specified, role in the control and modulation of emotional behavior. Since a specific experimental task which attempted to isolate prosodic semantics was not utilized in this experiment, only speculative inference can be provided as to the role of semantics in the system supporting prosody production.

It is reasonable to consider the possibility that the prefrontal regions have some involvement with semantic processing, of which emotion also plays a role. If this speculation is correct, these emotional semantic representations likely exist in a distributed network. Part of that distributed network may encode the prosodic pitch changes associated with a particular emotion. For instance, the representation for angry may include memories of angry facial expressions, actions, angry words, gestures, and even angry tones of voice. As noted earlier, this region may contain prototypic prosodic echoic representations for particular emotions. Blonder and colleagues (1991) suggested that these emotional semantic representations might be separate from their lexical or modular emotional components. They provided evidence that while these semantic representations were likely to be bilateral, they suggested that the lexical or modular components were likely located in the right hemisphere.

Why did the right, but not the left prefrontal cortex activate during these tasks? Others have demonstrated that generating words with emotional connotations engage the left prefrontal cortex (Crosson *et al.*, 1999b), yet the production of emotional prosody in this dissertation activated the right prefrontal cortex during the expression of angry prosody. It is possible that the proximate neuroanatomic location and projections from the right prefrontal cortex (which is a nexus of those representations), and the right inferior frontal gyrus (which may facilitate the motoric instantiation), is the reason for the prominent right, not left, prefrontal activity that was noted to occur in this study.

Do Prosody Production and Comprehension engage the same Brain Regions?

The present finding of preferential engagement of cortices near the right frontal pole as a result of a emotion vs. neutral prosody production task compliments one facet of the ablation studies of Ross (1981, 1988) who documented prosodic production deficits after right frontal lesions. However, Ross (1981, 1988) also argued that prosodic comprehension was facilitated by right posterior regions.

Ross' (1981, 1988) hypothesis is difficult to integrate with the results of George *et al.* (1996) who revealed right frontal activity in a PET study, during a prosody comprehension task. One factor that may be important in reconciling these differences is that George and colleagues (1996) did not organize their results by emotional valence which may have minimized the right posterior activity. PET also has a fairly low spatial resolution and more subtle right posterior activity may have been present in the George *et al*. (1996) study, but was below their statistical threshold.

It is possible that Ross's (1981, 1988) conjecture of a role of the right posterior region in prosody comprehension was simply incorrect and that the system supporting prosody in the right hemisphere does not parallel the organization of the language system in the left hemisphere. Since prosody comprehension was not evaluated in this dissertation, the validity of this facet of his hypothesis was not formally assessed. However, Nishitani and Hari (2000) recently provided evidence from a magnetoencephalogram (MEG) experiment with normal subjects that the left Brodmann's area 44 is a action execution/observation matching system. This is based on Rizzolatti and Arbib (1988)'s earlier conjecture of the existence of "mirror neurons" in this region. They discovered in the monkey that these neurons discharge either when a particular hand gesture is performed, or when that monkey observes that particular gesture. Rizzolatti and colleagues (1988) posited that these mirror neurons provide a mechanism for learning motoric hand gestures. They also suggested that this system supports the process by which we acquire representational language. Through observing and mimicking the motoric oro-facial and oro-linguial gestures of others, the discharges of these mirror neurons may enable the individual to match their speech productions to an earlier experienced motoric pattern. If this conjecture is correct, then Brodmann's area 44 in the right hemisphere might also contain mirror neurons which discharge when a particular prosody is produced, or when that intonation pattern is perceived. One could further speculate that the language system in the left hemisphere expands in development posteriorially from this Broca's area core to form the normative Broca's/Wernicke's continuum in proportion to the final representational complexity of this very advanced system. Since prosody is apparently utilized for fairly simple representational purposes, this expansion is more limited. It is known that the prosodic comprehension system becomes functional much earlier in development in contrast to the propositional language system (Bell, Davis, Morgan-Fisher, & Ross, 1990), which may indicate that it is a simpler, less complicated system with a less extensive cortical representation.

What is the Significance of the Right Posterior Cingulate Activity?

It is interesting to compare the posterior cingulate activity in this present study (see Figure 14) with that of a recent fMRI experiment by Maddock and Buonocore (1997). They reported strong left posterior cingulate gyrus activity when threat words were presented auditorily compared to neutral words. The posterior cingulate consists of Brodmann's areas 29, 20, 23, and 31 and contains neurons that monitor eye movements and respond to sensory stimuli. However, Brodmann's area 23 was the only significantly active region of the posterior cingulate that was noted in the angry vs. neutral comparison of this study. Ablation studies suggest that this region is involved in the modulation of attention, spatial orientation and memory (Sunderland and Hoesing, 1993; Valenstein *et al.*, 1987). Studies have also shown that the posterior cingulate cortex has extensive connections with the orbitofrontal cortex and the medial temporal region (Voyt and Pandya, 1987). It is likely that connections between posterior cingulate and parahippocampal cortices (Goldman Rakic, Selemon, & Schwartz, 1984; Musil and Olsen, 1993) play a role in processing episodic memories.

Lindfield, Wingfield, and Goodglass, 1999) demonstrated that emotional prosody boosts comprehension of lexical elements. It is possible that the undulating F_0 shifts in a speaker's voice which represent prosody, may be utilized to focus the attention of the listener. One could suggest that prosody helps to maintain a stable attentional channel between listener and speaker which may also increase the memorability of the communicative interaction. The right posterior cingulate, in conjunction with the right prefrontal region, may work to bind these elements into a memorable episodic event.

Why would the Right Angular Gyrus Activate during Prosody Production?

The left angular gyrus is known to integrate visual and somesthetic information necessary for reading. It is thought that the left angular gyrus is a central area involved in the processing of orthographic lexical word-forms. For instance, damage to this structure induces alexia with agraphia (Dejerine, 1891). However, the capabilities associated with the right angular gyrus have not been well established.

It may be that the right angular gyrus has a similar decoding/storage function to that of the left angular gyrus, although with a different focus reflecting the dominant capabilities of that hemisphere. For instance, while the left hemisphere is specialized for language and sequential problem-solving, the right hemisphere is believed to be specialized for attentional monitoring and visuospatial tasks (Gazzaniga, 2000). Therefore, one possibility is that the right angular gyrus provides a graphemic/prosodic decoding/storage function and associates these words with associated prosodic representations.

Conclusion - Research Question 2

Based on the preceding discussion, the broad outlines of a cognitive model of emotional prosody can be suggested based on the evidence in this dissertation, at least with respect to the angry prosody trials. As noted earlier, because of the potential confounds associated with the happy vs. neutral comparison reviewed in the preceding section, this conclusion is limited to the angry vs. neutral findings.

The process by which a subject produced a single angry utterance could be suggested based on this hypothetical model and integrated with the empirical evidence. For instance, the subject would first be presented with the written sentence and a cued emotion, such as angry. They would have to decode the written sentence and the prosodic cue and then access an echoic representation for angry prosody. This graphemic/prosodic decoding process might account for the activity in the right angular gyrus. This might have provided access to prosodic semantics located in the right prefrontal area. This region likely contains memory traces of past angry experiences, angry tones of voice etc. While this cortical processing occurred, a memory/attentional system might have been engaged to maintain these on-line representations through networks associated with the right posterior cingulate. Finally, a motoric sequence which represented the production of angry prosody would have been selected by engaging the prosodic output module located in the right middle frontal/premotor region. The module is hypothesized to contain the sequence of muscular adjustments necessary to produce angry prosody verbally. It is posited that this supra-segmental information would then be shared, via the corpus callosum, to Broca's area in the left hemisphere. Then this information would be passed down to cortico-bulbar tracts to facilitate the final motoric production via oral/lingual musculature. This would require the co-creation of a string of phonemes with a coherent syntactic structure (left frontal), which were overlaid with prosodic nuance (right frontal).

Clinical Implications

While this study examined the patterns of brain activity among neurologically intact individuals, the findings of the angry vs. neutral comparison also help explain the potentially disruptive effects of aprosodia on the lives of those who suffer right hemisphere injury. For instance, clinically the flat affect of right hemisphere patients is often misinterpreted as a sign of depression by health care workers. Knowledge of the difference between affective disorders and aprosodia as a result of neurological injury can help in the process of assessment.

These findings support what experienced clinicians already know, that it is always appropriate to assess emotional prosody in patients with right hemispheric injury and to treat these more subtle communication deficits (for example see Stringer, 1996). This information could be used to inform families of potential mismatches between the internal emotional experience of the patient and their possibly limited repertoire of emotional expressions utilized in verbal communication. This mismatch has the potential of hindering the patient's ability to effectively communicate in the home setting and provides a handicap in social situations. The co-occurrence of a deficit in prosodic comprehension further aggravates this situation.

Finally, these results compliment a recent study by Etcoff, Ekman, Magee and Frank (2000) which demonstrated that left hemisphere patients with aphasia were significantly more accurate than controls at detecting lies based on either facial or vocal cues. This suggests that damage to the networks underlying language comprehension may result in the development of compensatory skills in recognizing non-verbal behavior, possibly located in the intact right frontal lobe.

Future Research

Further advancement of statistical and methodological techniques such as rapid, random event-related fMRI (Burock, Buckner, Woldorff, Rosen, & Dale, 1999; Grabowski & Damasio, 1996) will help depict the complex patterns of brain activity associated with overt speech production. While the recent study by Barch *et al.*, (1999) validates the use of overt speech in a fMRI experimental paradigm, they do not recommend the use of single subject analysis. They argue that group analysis are still required because of limited statistical power at the individual subject level. However, it would be optimal to observe the patterns of fMRI activity for single subjects, especially with respect to studies of neurological patients with aprosodic deficits. The techniques developed for this dissertation have helped to lay the foundation for single subject studies which will examine those *in vivo* patterns in more detail. The most promising future studies will probe the patterns of brain activity originating from patients who demonstrate aprosodia after brain lesions. Detailed behavioral assessment of these aprosodic patients can be correlated with *in vivo* fMRI brain activity and compared with normative patterns of brain activity from subjects that have not sustained neurological injury. Then detailed comparisons can be made between the production of non-linguistic (emotional and non-emotional) and linguistic prosody to better characterize these relationships.

Finally, these techniques will permit the examination of the changing patterns of brain activity associated with the natural course of recovery after neurological injury. These techniques potentially will allow comparisons between the networks engaged before and after treatment, thereby providing a technique to assess the efficacy of various treatment strategies.

Summary

The finely spatial resolution of fMRI has permitted an extension of the main finding of landmark neurological studies (Tucker, Watson, & Heilman, 1977; Ross & Mesulam, 1979) which revealed a role of the right hemisphere in the production of emotional prosody. These *in vivo* findings with normal subjects has provided further support for their right hemisphere dominance theory and provided tentative evidence that a prosodic output module may be operative in the right frontal lobe.

APPENDIX A
PRE-SCAN SUBJECT CHECKLIST

1. Name? ______________________________
2. Age? ____________________________________
3. Date of Birth__________________________
4. Weight (for setting scanner parameters)________________
5. Email address (to send tif image to) _______________________
6. Mailing address (to send glossy image to)________________________
7. Have you had a history of long lasting (chronic) depressions or psychiatric illness? Any history of this in your immediate family? ______________________
8. Have you ever had a significant injury to your head, loss of consciousness, possibly after an automobile or a bicycle accident? _________________________
9. Any history of a learning disorder, dyslexia, or a attention deficit disorder?

____

10. What is the highest educational degree you have obtained? __________
11. Is English the first language you learned to speak? Do you speak any other languages and at what age did you acquire them? ____________________
12. What is your ethnic background (country of origin of your parents or grandparents)? ___________________
13. Have your ever worked as a professional actor/actress, DJ? ______________

APPENDIX B
SUBJECT'S POST-SCAN QUESTIONNAIRE

1. When you were in the scanner and asked to produce a happy tone in your voice, do you think it actually sounded happy? ______________________________
2. When you were saying the sentence with happy prosody, did you actually "feel" happy, or did your voice only sound happy?

   ____
3. When you were in the scanner and asked to produce a neutral tone in your voice, do you think it actually sounded neutral? If you think it sounded emotional, which emotion was it closest to? ______________________________
4. When you were saying the sentence with neutral prosody, did you actually "feel" emotionally neutral, or did your voice only sound emotionally neutral? If you didn't feel emotionally neutral, which emotion were you experiencing?______________________
5. When you were in the scanner and asked to produce an angry tone in your voice, do you think your voice actually sounded angry?

   ____
6. When you were saying the sentence with angry prosody, did you actually "feel" angry, or did your voice only sound angry?

   ____

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Jeffrey Michael Anderson was born on February 16, 1957, in Glen Cove, New York. In 1975 he graduated cum laude from Northeast High School in Saint Petersburg, Florida. He graduated cum laude with a Bachelor of Arts degree with a major in psychology from Gordon College, Wenham, Massachusetts, in 1985. He received his Master of Arts degree in communication processes and disorders in 1993 from the Massachusetts General Hospital Institute of Health Professions, in Boston, Massachusetts. After completing his master's degree he was a Research Speech Pathologist in the Cognitive Neuropsychology Laboratory of Dr. Alfonso Caramazza, Dartmouth College, Hanover, New Hampshire. At the invitation of Dr. Heilman, he came to the University of Florida in August 1995 to pursue a Doctor of Philosophy degree in the department of Communication Sciences and Disorders. He received his Ph.D. in August 2000. Upon completion of his degree he commenced a postdoctoral fellowship at Harvard Medical School/Massachusetts General Hospital-NMR Center in Boston, Massachusetts. Dr. Anderson is married and the father of two sons.

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.

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